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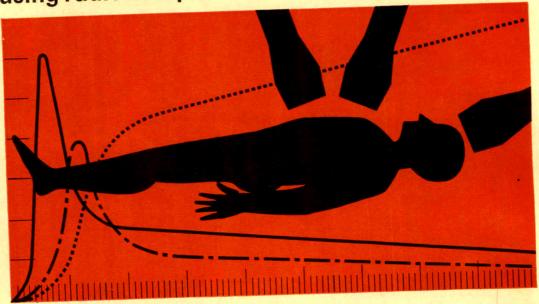
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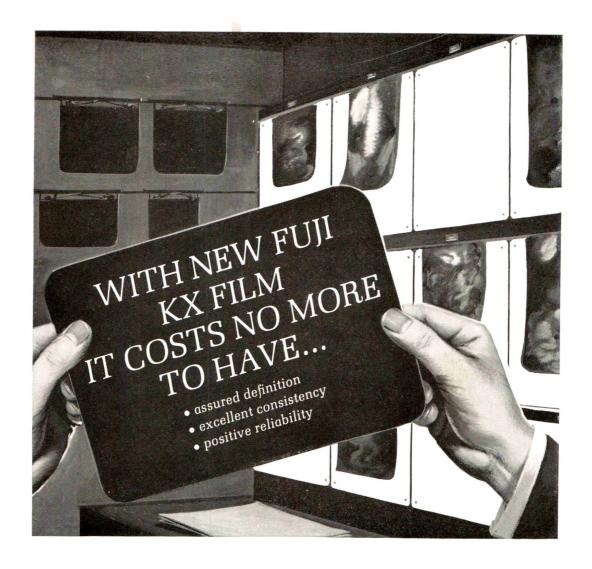
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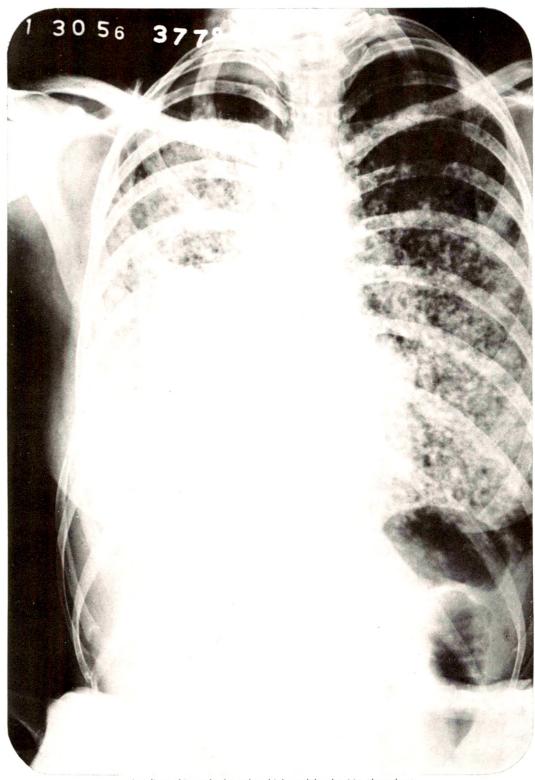
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A radiographic study showed multiple nodular densities throughout both lung fields with evidence of coalescence in the right lower lobe.

Why did this woman have dyspnea on Thanksgiving Day and again on Christmas?

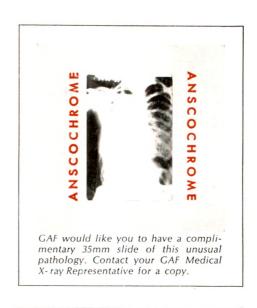
A 39-year-old woman had been well until Thanksgiving Day when she complained of shortness of breath. It disappeared—recurred on Christmas Day—and disappeared again. Thirty days later she was admitted with continuous and marked dyspnea that had appeared three days before admission. She had lost 20 pounds in the previous six months.

Physical examination revealed dullness and vocal fremitus with some wheezes and diminished or absent breath sounds over the right base posteriorly. Just above this area there was definite bronchial breathing.

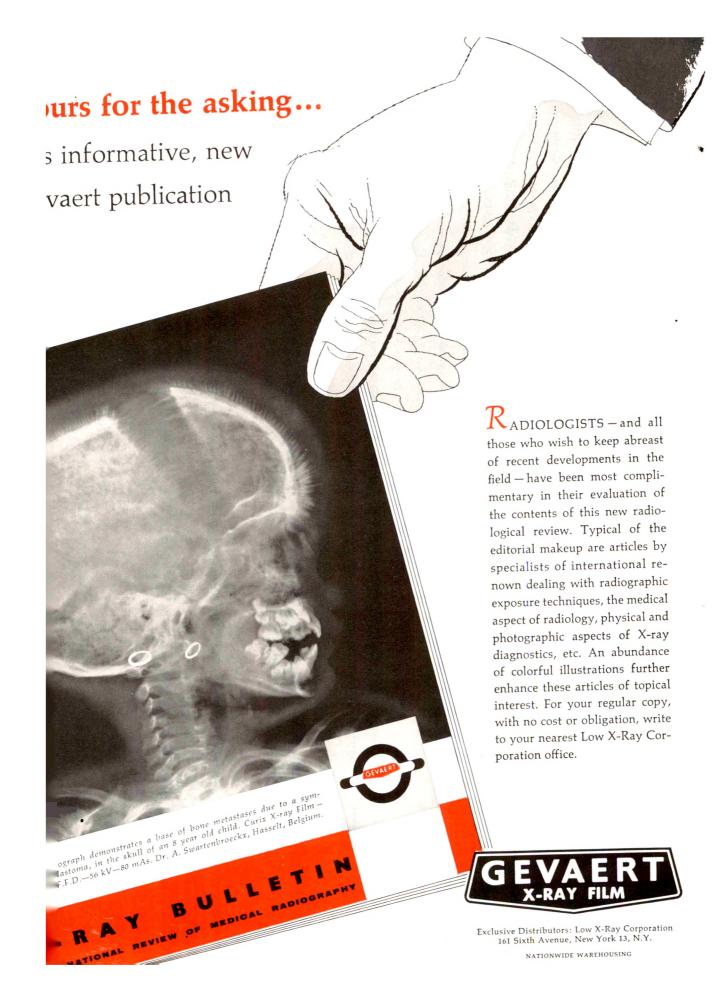
Radiographic studies showed multiple nodular densities throughout both lung fields —with evidence of coalescence in the right lower lobe. Retraction of the heart and mediastinum to the right seemed due to partial collapse of the lung. The findings suggested three possibilities: bronchiolar carcinoma, diffuse metastatic disease and fungus infection.

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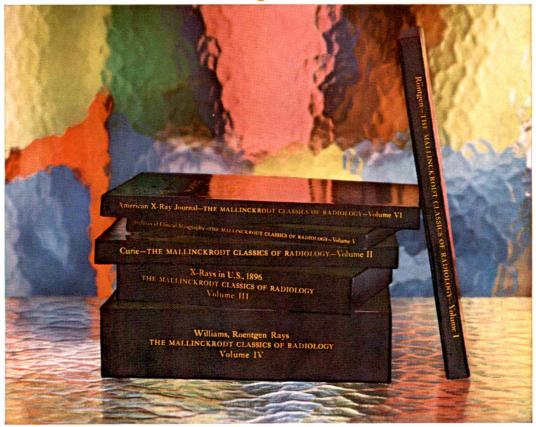
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- Volume IV. "The Roentgen Rays in Medicine and Surgery," by F. H. Williams, 1901
- Volume V. "Archives of Clinical Skiagraphy," Volume I (4 numbers), 1896
- Volume VI. "The American X-Ray Journal," Volume I (5 numbers), 1897

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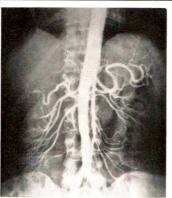


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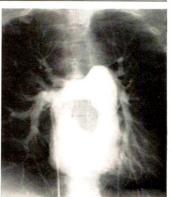


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for intravenous urography, intravascular angiocardiography and aortography

Product Particulars

CONRAY: Each ml. contains 0.6 Gm. meglumine iothalamate; not more than 0.11 mg. calcium disodium ethylenediaminetetraacetate as stabilizer; not more than 0.15 mg. sodium biphosphate as a buffer.

Angio-CONRAY: Each ml. contains 0.8 Gm. sodium iothalamate; not more than 0.135 mg. calcium disodium ethylenediaminetetraacetate as stabilizer; not more than 0.15 mg. sodium biphosphate as a buffer.

CONRAY-400: Each ml. contains 0.668 Gm. sodium iothalamate; not more than 0.135 mg. calcium disodium ethylenediaminetetraacetate as stabilizer; not more than 0.15 mg. sodium biphosphate as a buffer.

Side Effects: With CONRAY (meglumine iothalamate 60%) these have been minor and infrequent, and include nausea, vomiting, urticaria, However, as with any iodinated intravascular contrast agent, the possibility of severe reactions exists (neurological complications, the so-called anaphylactic response and cardiovascular collapse). With Angio-CONRAY (sodium iothalamate 80%) and CONRAY-400 (sodium iothalamate 66.8%) rapid injection has produced a wave of warmth or heat passing over the body, often associated with flush. Other transient reactions infrequently observed are nausea, vomiting and bitter taste. In rare instances, injection of a con-

trast medium has been reported to produce more serious reactions including fatalities. *Note:* Because of the possibility of severe reactions to any medium, patients should not be left alone for at least 15 minutes following injection.

Caution: CONRAY-400 (sodium iothalamate 66.8%) and Angio-CONRAY (sodium iothalamate 80%) are not intended for use in cerebral angiography. For this purpose, CONRAY (meglumine iothalamate 60%) is recommended.

Contraindications: For all three media, caution is required in cases involving severe systemic disease. In patients with advanced renal disease, use with caution and then only when need for examination dictates. In patients with a history of allergy or those exhibiting a positive reaction to the sensitivity test, drugs and facilities for emergency use must be readily available.

Precautions: For Angio-CONRAY (sodium iothalamate 80%) and CONRAY-400 (sodium iothalamate 66.8%), cardiac arrhythmias, including ventricular fibrillation, have been reported with the use of these media in procedures for visualizing the heart and its associated large vessels. Such occurrences may be associated with situations in which appreciable amounts of relatively undiluted medium enter the coronary circulation. Facilities for immediate treatment of such reactions should be available.





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Joseph Pen-Tze Lin, M.D.—New York University School of Medicine

Mario Ramos, R.T., N.Y.U.—Bellevue Medical Center Ebel Guzman, R.T., N.Y.U.—Bellevue Medical Center

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Sacrum

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Radiographic Examination

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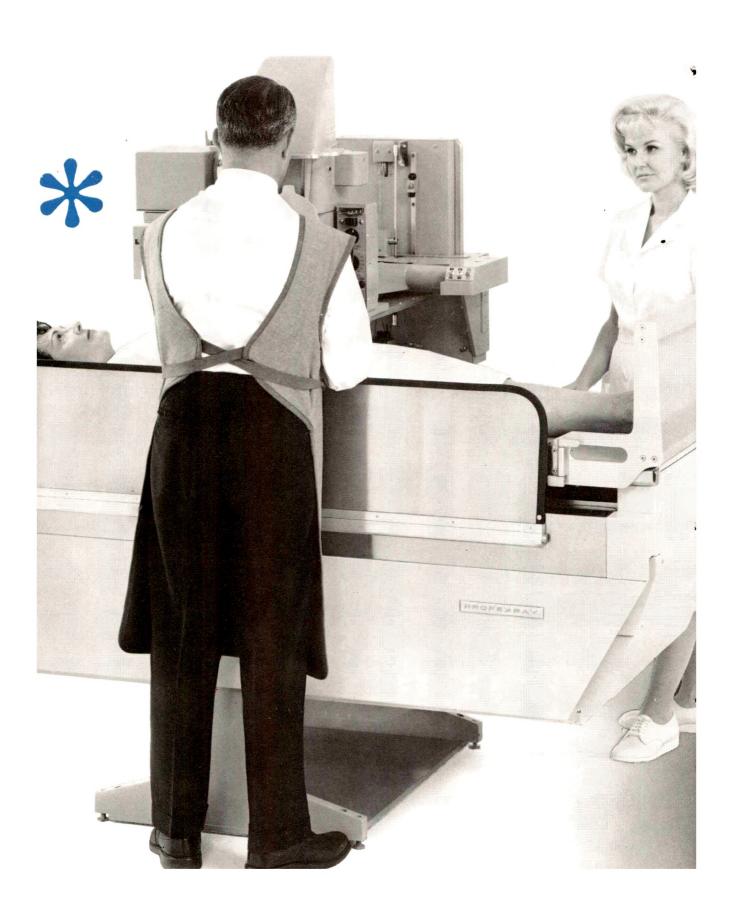
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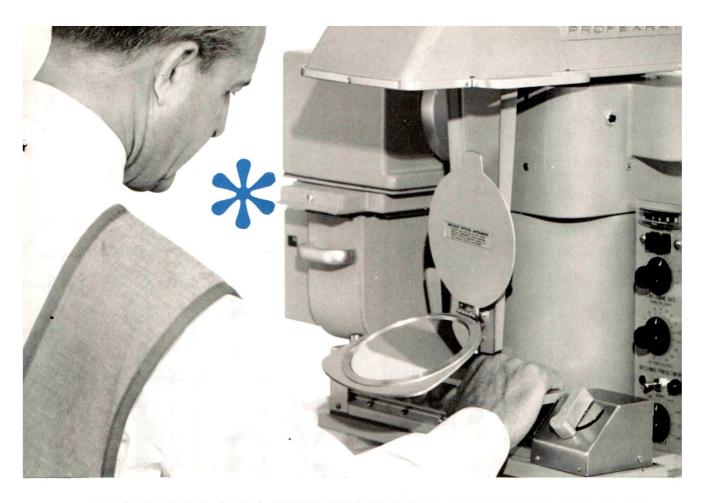
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- 4. Three smooth motor drives are available: single-speed, dual-speed, or continuously variable speed.



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Provides records (spot films) of the intensified fluorosco image with a degree of definition not obtainable with convitional spot films: (1) at intervals controlled by operator, (2) sequentially at rates up to six exposures per second

FLEXIBILITY

- 1. May be used with or without spot film device—t significant advantages are to be gained when used place of spot film device.
- 2. Exposure factors to record the fluoroscopic image a 1/10 to 1/20 of those used for regular spot film studi. These lower factors permit the use of a fractional-foc tube, resulting in films of unparalleled sharpness. Mag fication studies become routine.
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THE MEVATRON "8"

AN 8 MeV 360° ROTARY MEDICAL LINEAR ACCELERATOR THAT PROVIDES

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8

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The Mevatron 8 is based on Applied Radiation's more than ten years' experience. We are the only company engaged exclusively in the design and

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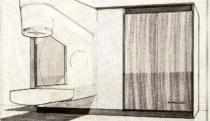
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The first two Mevatrons are now being readied for the Albert Einstein College of Medicine, Yeshiva University, New York and the Methodist Hospital in Houston, Texas. You're invited to our open house on September 26, during the American Roentgen Ray Society Conference to see these units during final assembly and test. We have arranged for transportation to our plant in Walnut Creek, a pleasant 20 minutes from downtown San Francisco.

Specifications are detailed in the catalog following this ad-





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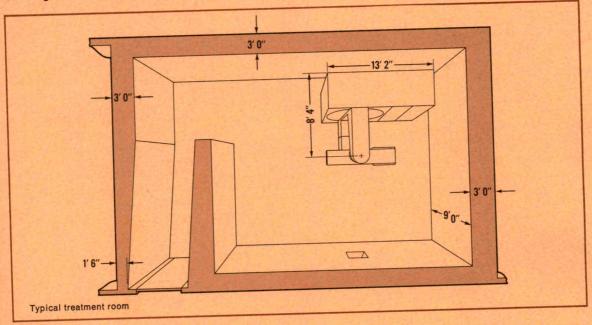
vertisement. For information on fitting the Mevatron to your specific requirements, write us at Walnut Creek, California, 94596. Or call us at (415) 935-2250.

APPLIED RADIATION

Treatment Room

The Mevatron 8 is relatively compact, despite its high output capabilities, and will fit in most existing treatment rooms. A typical room is

shown below. Applied Radiation provides all necessary aid in planning new treatment rooms, including detailed drawings of typical arrangements already in use.



OPERATING SPECIFICATIONS

Automatic	Clinical C	peration
------------------	------------	----------

Roentgen Outputs: At 6 MeV	400 R/minute at one meter, Flattened – X-rays250 R/minute at one meter, Flattened – X-rays
At 8 MeV Electron beam power	500 watts at 6 MeV

Licotron boam p		
Manual Research Operation X-Rays — 7 MeV	Unflattened	Flattened
Measured at one meter:	2000 R/Min	1000 R/Min 500 R/Min
Straight through beam Bent beam Maximum Electron Beam Power at 7 MeV: Straight through beam Bent beam	1300 watts	

General - Automatic and Manual Operation

General - Automatic and Manage of	2-10 MeV Push-button selectable in 1 MeV steps.
Energy range	3-10 MeV. Push-button selectable in 1 MeV steps
Focal spot diameter	Within +2 5% over a 30 cm x 30 cm field
Field flatness	0 x 0 cm to 30 cm x 30 cm at 100 T.S.D.
Field size	4 microseconds
Pulse length	
Pulse repetition rate	
Rotary Mount	390°

Rotary Mount Total Angle of rotation	390°
Total Angle of rotation	Continuously variable 18° to 360°/minute
Speed of rotation	. Gontinadady random 100 cm
Target to axis of rotation	

For additional information about the Mevatron 8 and how it can fit your radiotherapy and research requirements write Applied Radiation Corporation at Walnut Creek, California. Or call (415) 935-2250.

APPLIED RADIATION

WALNUT CREEK, CALIFORNIA 94596 / TEL.: (415) 935-2250 / TWX: (415) 933-9103

Exact Dose Rate Control

The Mevatron 8, compared to lower energy machines, provides:

- 1. Increased depth doses
- 2. Reduced skin entry doses
- Less scattered radiation outside the defined field
- More uniform radiation of heterogeneous tissues.

The high X-ray output of the Mevatron also allows the use of long target-to-skin distances while keeping treatment time short.

During treatment, dose rate is constantly monitored and automatically stabilized. Digital read-out dials show total and instantaneous dose on the control console.

A pre-set Total Dose Selector and Back-up Timer are adjusted before treatment. They indicate original treatment setting and act as a "fail-safe" system for the standard dose control.

Accurate Beam Shaping

The focal spot on the Mevatron 8 has a diameter less than 3 mm. It is virtually a point source of radiation, for precise beam shaping with minimum penumbra. Extremely narrow, pencil-like beams can be used, as well as a variety of field shapes and sizes, for accurate coverage of the exact tumor area.

Maximum field size is 30 cm x 30 cm at 1 meter target-to-skin distance. Field flatness is ± 2.5% and radiation leakage outside the primary beam is less than 1%. Field size is shown on digital read-out dials on the face of the collimator. Other features include a light source that coincides with the X-ray beam, optical front and back pointers, and an optical distance indicator.

Positive Beam Control

Besides Automatic Frequency Control for energy stability, and automatic dose rate

stabilization, there is also continuous monitoring and automatic stabilization of other important operating parameters, such as beam current and central beam axis position. This assures greater positional stability and uniformity of the field at the patient.

Precise Rotation Therapy

Rugged construction of the main rotation system on the Mevatron 8 provides vibration-free movement. The boom containing the waveguide is mounted on a massive, precision-machined drum, supported by heavy-duty rollers. Drive mechanism is servo-controlled and damped for accurate alignment and travel without overshoot. Optimum rotational beam position and dose rate accuracy are assured by this type mounting and damped servo construction.

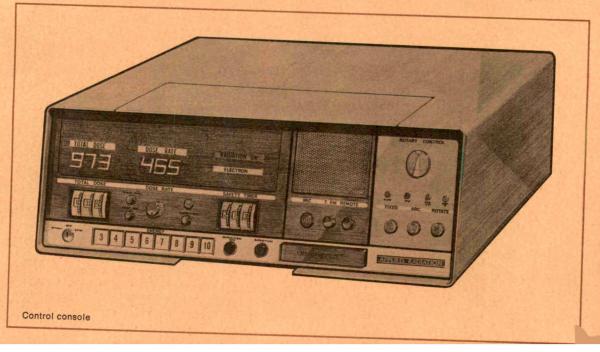
Special front panel controls permit programming the rotation system to accelerate and decelerate outside the treatment arc. The beam is turned "on" and "off," automatically, at the limits of the pre-set arc while the head is traveling at its precisely programmed speed. An important optional feature is the new anti-

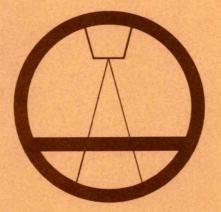
An important optional feature is the new anticollision system. A special detection circuit senses the proximity of the patient or the couch, and automatically stops the machine before accidental contact.

Electron Therapy Capability

The electron beam of the Mevatron 8 is designed for optimum treatment of tumors at or near the skin surface.

The maximum range in tissue of high-energy electrons is about 0.5 cm per MeV. Unlike Grenz rays or low energy X-rays, they cause maximum dose to occur below the radiosensitive skin surface. The thickness of surface to be treated can be controlled by adjusting the electron beam energy, minimizing effects





The Mevatron 8 incorporates Applied Radiation's more than ten years' specialized experience in the design and production of linear accelerators. It has all the features needed for precise radiation therapy, and capabilities for specialized medical research applications.

Features of the Mevatron 8 include:

For Routine Therapy

Simple Automatic Control
Precise Control of Variable Energy
Exact Dose Rate Control
Accurate Beam Shaping
Positive Beam Control
Precise Rotation Therapy
Electron Therapy Capability
Retractable Beamshield
Choice of Treatment Couches
Reliable Operation, Easy Maintenance

For Medical Research

Flexible Manual Control
High X-Ray Output – Specialized Therapy:
Hyperbaric Oxygen Therapy
Whole Body Irradiation
High Electron Output – Horizontal Beam
Electron Sterilization
Electron Research
Neutron Production
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Research Program Consulting

ROUTINE THERAPYWITH THE MEVATRON 8

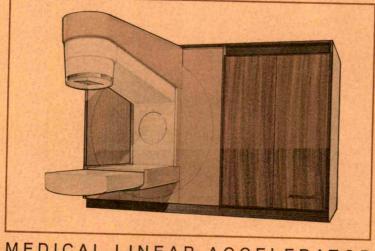
Simple, Automatic Control

Controls on the Mevatron 8 are simple and safe, easily operated by any technician familiar with standard X-ray equipment. Clearly labelled pushbuttons and dials monitor and control every key operation. There's also an advanced Fault Read-Out Panel that visually warns the operator if a malfunction occurs in any part of the system. Control console is solid-state and requires less than 2.5 cubic feet of space.

Precise Control of Variable Energy

Energy levels on the Mevatron 8 – from 3-10 MeV – are pushbutton-selectable in one MeV steps, and an Automatic Frequency Control continuously stabilizes energy at the pre-set level during treatment. It also makes automatic fool-proof selection of the correct beam flattening filter for the particular energy level. With the variable energy of the Mevatron 8, treatment techniques and variation of percentage depth doses can be selected for each specific case. In addition, the effects of energy variation on treatment techniques can be demonstrated for teaching purposes.

the MEVATRON



MEDICAL LINEAR ACCELERATOR



MEDICAL RESEARCH -SPECIALIZED TECHNIQUES

Flexible Manual Control

Manual controls for the Mevatron 8 are located in the top of the console with safety locks to prevent operation by unauthorized personnel. With the manual mode of operation the dose rate may be increased to over five times its rated value, or more than 2000 R/min. This manual flexibility allows selection, in varying degrees, of dose, pulse repetition rates, and gun emission values. It also allows programming of the unit for specific applications, and provides manual back-up of the automatic controls.

High X-Ray Output - Specialized Therapy

When high X-ray outputs are needed for specialized therapy the Mevatron is operated manually, with the beam bent as for normal clinical operation.

With beamshield retracted and couch removed, techniques such as hyperbaric oxygen therapy and whole body irradiation can be used. During hyperbaric oxygen therapy the complete treatment cycle, from initial pressurization through set-up, treatment, and final decompression can be shortened by the availability of high dose rates and precision control. Shortened treatment cycles lessen patient strain and reduce the possibility of trauma.

High Electron Output - Horizontal Beam

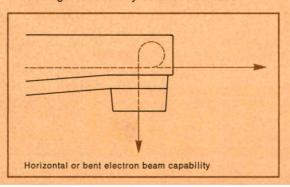
The treatment head of the Mevatron 8 is designed to allow quick changeover to a horizontal electron beam. A drift tube can be used to bring the electron beam out to an adjoining room. Electrons, X-rays, and neutrons can thus be used outside the treatment room.

Electron Sterilization

The high electron output of the Mevatron easily produces the massive doses required for bone and tissue sterilization. It can also be used to sterilize hospital supplies, sutures, and surgical instruments.

Electron Research

An important use for the electron output of the Mevatron 8 is the study of radiation effects on medical, biological, chemical, and physical systems. In vivo and in vitro radiation studies can also be carried out by use of a wide range of carefully controlled doses.



Neutron Production

Only a short time is needed to convert the Mevatron 8 from therapy to a neutron-activation program. Neutrons are produced by X-rays in a photonuclear process on a beryllium or deuterium target. Removal of the collimator is not necessary for this operation.

Radioisotope Production

Another important use of the Mevatron 8 is in production of short-lived isotopes, for analysis, diagnosis, or therapy. Some are listed on the accompanying table. Many have such short lives that it is impractical for hospitals to obtain them in any other way, either because there is no reactor available or because the time required to obtain them from a reactor is longer than the particular isotope decay time. Also, some isotopes can only be made with an accelerator.

Selected List of Isotopes Produced with the Mevatron 8

Isotope Formed	Specific Activity μC/gr	Half-Life
Ae-28	10	2.4 min.
Br-80	25	18 min.
CI-38	5	37.5 min.
F-20	1	12 sec.
Hg-199	35	43 min.
I-129	70	25 min.
In-116	1000	54 min.
Mg-27	0.3	10.2 min.
Mn-56	85	2.6 hr.
Na-24	2	14.8 hr.
V-52	100	3.7 min.
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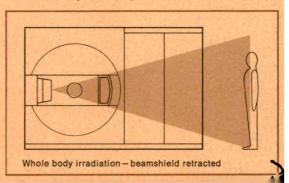
Basis:

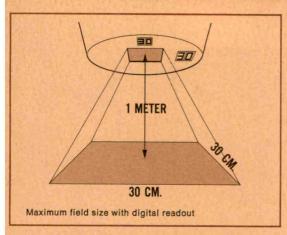
Thermal-neutron flux of 10⁸ n/sec-cm². Bombardment time is one hour.

Research Program Consulting

Applied Radiation has pioneered many firsts in the linear accelerator field . . . the first commercially produced linear accelerator, the first accelerators for electron beam processing and flash radiography, and the first accelerator for the radiography of guided missiles.

A highly skilled staff, and consultant specialists are available for every phase of a medical linear accelerator installation program, from initial concept to completion of the installation.





on skin surface and bone marrow. X-ray contamination of the electron beam is minimal (less than 0.1%).

An electron-beam reduction circuit reduces the beam by a factor of over 1000 and provides a very low power, highly stabilized output during normal electron therapy. When maximum electron dose rates are needed, the reduction circuit can be by-passed by the manual mode of operation.

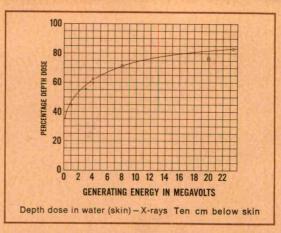
Retractable Beamshield

The Mevatron 8 has a motorized beam-shield that reduces room shielding needs by 60%. At treatment distances over one meter, it can be retracted out of the beam.

A prohibited-sector cam on the rotating assembly prevents irradiation of insufficiently shielded areas when the beamshield is retracted. The Mevatron 8 can also be supplied without the beamshield.

Choice of Treatment Couches

Several types of isocentrically mounted couches are available. They can be an integral part of the machine or supplied with a

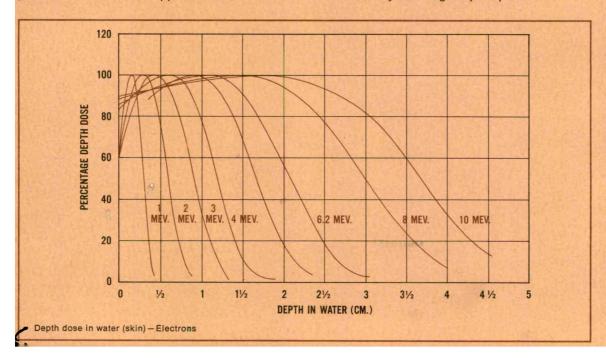


removable top and retractable support to allow use of a separate treatment system, such as a hyperbaric oxygen therapy tank.

Reliable Operation, Easy Maintenance

Important reliability, maintainability, and service improvements in the Mevatron 8 optimize performance dependability. Among these are:

- 1. Reliability through:
 - a. Extensive use of solid state electronics.
 - b. Exclusive use of components rated well above their machine usage.
 - c. Advanced testing and quality control programs.
 - d. Simplified preventive maintenance programs.
- 2. Maintainability through:
 - a. Front panel fault readout and detection.
 - b. Modular component layout for easy access.
 - A comprehensive factory training course for customer technicians.
- 3. Service through:
 - a. A factory service group, with world-wide centers
 - b. Factory stocking of spare parts.



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ROENTGENOLOGIC EVALUATION OF RENAL TRAUMA WITH EMPHASIS ON RENAL ANGIOGRAPHY*

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NEW YORK, NEW YORK

A MAJOR problem in consideration of renal trauma has been a proper assessment of the extent of injury in order to decide on the correct method of treatment and to evaluate the kidney's capacity for recovery. In any such evaluation, there must be an accurate classification of the injury.

There are three major types of injury which lead to damage to the kidney:

- 1. Blunt trauma, such as:
 - (a) Direct blows to the flank or abdomen as in athletics.
 - (b) Falls with injury to the abdomen.
 - (c) Automobile accidents with the patient being an occupant of the vehicle in collision or a pedestrian struck by a car.
- 2. Penetrating wounds from bullets or stab injuries.
- 3. Operative injuries, such as:
 - (a) In the course of instrumentation.

 The most common mechanism here is retrograde catheterization, usu-

ally with perforation of the fornix of a cranial calyx. Fortunately, this type of injury, although not uncommon, is usually of minor consequence.

- (b) In the course of percutaneous needle biopsy of the kidney.
- (c) Injury to the renal parenchyma in the performance of bisection of the kidney as in the removal of renal calculi.
- (d) Inadvertent ligation of a major intrarenal artery in the surgical treatment of a kidney laceration.

As expected from some of the mechanisms of injury, there is a preponderance of young males in any series analyzing renal trauma. In Liska's group of 81 patients, 15 62 per cent were below 31 years in age and 86 per cent of the 81 patients were males. Nilsson and Sandberg²⁰ reported 62 patients; 58 per cent were below the age of 30 and 79 per cent of the total number were males. In McCague's 19 series of 67 patients,

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58 per cent were below the age of 31 and 88 per cent of the total number were males.

The most common clinical indication of damage to the kidney following trauma is the presence of hematuria, gross or microscopic. However, 10 to 25 per cent of patients with renal injury do not have hematuria. The absence of hematuria does not necessarily indicate minor injury since blood may not appear in the urine in such grave conditions as traumatic thrombosis of the renal artery or avulsion of the ureter from the pelvis. Also, the ureter may be blocked by blood clots. Other clinical findings, although not due necessarily to renal injury, include: the presence of a mass in the flank, abdominal or flank pain and tenderness.

CLASSIFICATION

Several methods of classification have been introduced to indicate the extent of injury to the kidney. Unfortunately, any classification short of the findings at nephrectomy or autopsy may prove incorrect. Even findings at surgical exploration with inspection of the external surface of the kidney and its bed cannot always give a full assessment of the damage.

Methods of classification include: pathologic-anatomic, clinical, roentgenologic and follow-up. For the most part, each method categorizes three degrees of injury: minor, major and catastrophic (or critical).

The pathologic-anatomic method attempts to evaluate the degree of anatomic injury from various diagnostic procedures; this, however, is frequently inconclusive in the absence of direct inspection of the kidney. Minor injury refers to contusion without disruption of the calyceal system and without a break in the renal capsule. Break in the renal capsule or into the calyceal system constitutes major injury. The catastrophic group includes: shattered kidney, tears of the ureter or vessels in the renal hilus, or infarction of the kidney.

In the clinical classification, short-lasting hematuria, subsiding in a few days, with normal vital signs indicates minor injury. No flank masses are palpable. Major injury includes gross hematuria for several days, severe pain (abdominal or lumbar), and a palpable mass. There may be a progressive slow deterioration of the patient's condition due to blood loss. In catastrophic injury there is rapid onset of shock. By these criteria traumatic thrombosis of the renal artery would not receive its due seriousness.

Roentgenologic classifications have been based primarily on the findings at intravenous urography. The following findings suggest only minor injury: normal renal and psoas outlines; normal intravenous urogram or at most minimal distortion of the calyces which could be due to intrarenal hematoma or edema. Diminished concentration of the contrast medium on the involved side, delayed excretion, diminished excretory nephrogram, and filling defects (clots) in the renal pelvis may also be seen in the minor injury group. Evidence of perirenal hematoma or extravasation of the contrast medium (intrarenal or extrarenal) suggests major kidney injury. Of course, signs of retroperitoneal hemorrhage such as obliteration or diminution in the sharpness of the psoas or renal outline, or displacement of the kidney or upper ureter may result from bleeding of the other retroperitoneal structures without serious injury to the kidney. The renal pelvic architecture, if visualized, is reasonably well preserved. In catastrophic injury, as with the shattered kidney, there is marked deformity of the calyces with loss of pelvic architecture and gross extravasation of the contrast medium if excretion is visualized. There is massive perirenal hemorrhage. In cases of avulsion of the ureter, excretion of the contrast medium is often preserved with extravasation from the site of tear. In cases of acute thrombosis of the main renal artery, there is no excretion of the contrast medium at the time of urography; retrograde study, if done, will show a normal pyelogram.

A classification based on follow-up studies has, of course, no prognostic or therapeutic value. Those patients who show complete return to normal on urog-

raphy are considered to have suffered minor renal trauma. Major trauma refers to cases with residual urographic abnormalities or where complications result. In catastrophic trauma there is complete loss of kidney function or progressive deterioration of the patient due to the renal injury. In general, most patients with renal injury—manifested usually by hematuria—have suffered minor injury. Of all renal trauma cases, 60 to 65 per cent represent minor injury, 30 to 35 per cent represent major injury and 1 to 5 per cent catastrophic injury.

TREATMENT

It is unfortunate that no satisfactory classification is at hand since therapy has on occasion been based on an inaccurate estimate of the degree of injury. Everyone agrees that in cases with rapidly progressive shock, proof of ureteral or vascular tear at the renal hilus, or thrombosis of the main renal artery immediate surgery is indicated. In patients falling into the group of contusion, there is general agreement for conservative treatment. However, in patients with extravasation or perirenal hematoma (major trauma), there is support for both actions—surgery or conservative care.

If there is not immediate danger to the survival of the patient or to the function of the injured kidney, a consideration for surgical exploration within a few days of the injury is the possibility of late sequelae. Most injured kidneys return to normal in all studies; this is so because most renal injuries are of minor nature and also some major injuries probably go on to complete healing without surgical therapy. Yet the kidney may become completely atrophic, due most likely to severe parenchymal damage or to damage to renal vascularity. Scattered atrophic zones will be manifest as scars in the recovered kidney. The development of hypertension, occasionally reported as a late complication of kidney trauma, probably results from damage to renal blood vessels or possibly from constricting fibrosis following perinephric hem-

atoma. Also, perirenal or periureteral fibrosis may be present without hypertension; these changes most likely result from retroperitoneal collections of blood or urine. Obstructive hydronephrosis, involving the total kidney or a localized area can follow stricture after injury to the ureter, pelvis or an infundibulum. The traumatized kidney with intrarenal or extrarenal hemorrhage along with compromise of blood supply is a good medium for invasion by pathogenic bacteria, leading to pyonephrosis, pyelonephritis or abscess. A hematoma-intrarenal or extrarenal-may become calcified or may end up as a cyst with or without calcified walls. Hodges et al.11 considered 23 of their 71 patients to have suffered major renal injury. Of the 14 patients treated conservatively (nonsurgical methods), 12 (86 per cent) developed significant residual renal disease with later surgery required in 8 of these. They recommended early operative treatment in all instances of major injury. On the other hand, Sargent and Marquardt²⁷ reported 72 patients with major renal injury, 2 having been treated with prompt surgery. Of the remaining 70, treated conservatively, 61 showed good recovery with freedom from disabling or important demonstrable defects. This left 9 of the 70 (13 per cent) with significant sequelae. They recommended conservative therapy for most cases of major renal injury.

Olsson and Lunderquist²² maintained that the commonly used roentgenographic studies—abdominal roentgenogram, intravenous urogram or even retrograde pyelogram—frequently do not show the full extent of renal damage, with similar changes shown in kidneys with markedly different degrees of injury.

ROENTGENOGRAPHIC STUDIES

In the examination of a patient with presumed trauma to the kidney, several types of roentgenographic studies are commonly employed in search for specific findings suggesting renal injury.

ABDOMINAL ROENTGENOGRAPHY

A roentgenogram of the abdomen is obtained in all cases where feasible. In about 75 per cent of patients with renal injury, this study is normal, chiefly because most kidney injuries are minor. Obliteration or diminution in sharpness of the kidney or psoas muscle outline is evidence for retroperitoneal blood or urine. Unfortunately, this sign may be unobtainable because of overlying bowel gas or fluid contents in the unprepared, injured patient who may be suffering from ileus due to other abdominal injuries. The visualization of a soft tissue mass in the flank has similar significance retroperitoneal hematoma or urine collection. Scoliosis, concave to the side of injury, is related to irritation of the psoas muscle. However, these various signs—obliteration of kidney or psoas outline and scoliosiscould be due to retroperitoneal blood from other retroperitoneal injuries besides the kidney, as from spine fracture. The finding of fractures—low ribs or lumbar spinemerely suggests the severity of the injury with no indication as to involvement of the kidney. Elevation of the ipsilateral diaphragm dome has been described in patients with perirenal hemorrhage.

INTRAVENOUS UROGRAPHY

Intravenous urography has been considered to be the most informative roentgenologic study in patients with renal injury. However, this study too is frequently unsatisfactory in delineating the extent of injury. In the acutely injured patient, the immediate intravenous urogram has been reported to be of satisfactory diagnostic quality in only 30 to 50 per cent, and, where of satisfactory quality, correct in 50 to 80 per cent as to indicating the extent of renal damage. 5, 9, 24, 25 Absence of excretion of the contrast medium on the injured side may be seen with minor renal injury, but usually this is a finding in major or catastrophic injury. Hypotension from blood loss will not lead to nonexcretion from only one kidney; there is no conclusive support for the con-

cept of reflex anuria. The absence of excretion from one part of the kidney may be an indication of localized renal damage; to discover such localized deficiency in excretion, films are needed early in the course of an intravenous urography—2 to 5 minute films—to visualize nonopacifying calyces. In later films all the calyces will be opacified, the nonexcreting ones being filled by overflow from the renal pelvis. Also hypoconcentration of the opacified calyceal system may be an indication of renal injury.

Extravasation of the opacified urine into the renal parenchyma from the calyceal system is indubitable evidence of a break into one or more calyces. If the extravasation proceeds into the perirenal space, then the break also involves the external surface of the kidney; from the extent and shape of this perirenal extravasation may be determined whether or not the fracture includes the renal capsule. The intravenous urogram does not always demonstrate such fractures; retrograde pyelography may on occasion show an extravasation not seen at the time of the intravenous study.

The excretory nephrogram, best seen on the very early films of an intravenous urography $-\frac{1}{2}$, 1 or 2 minute film after rapid intravenous administration of the contrast medium—is a fairly good indication of renal function. A definite diminution in the intensity of the nephrogram on the injured side as compared to that of the contralateral kidney is good evidence of renal injury. Similarly, the nephrogram, if present, offers good visualization of the kidney for study of its size and position as well as of the clarity of its outline. The loss of nephrogram intensity gives no indication of the severity of the injury. In acute injury an enlarged kidney usually indicates intrarenal hematoma or edema; a small kidney might result from thrombosis of the main renal artery. Displacement of the kidney or loss of its outline usually speaks for perirenal collection of blood or urine.

The presence of calyceal or pelvic filling defects following trauma suggests blood

clots, which of themselves give no information as to the degree of injury. Blood clots can also produce obstruction in the ureter with the demonstration of the urographic signs of acute ureteral obstruction, provided the kidney excretes the contrast medium.

Distortion of the calyces or pelvis following trauma is most often due to compression by hematoma, intrarenal or extrarenal. Edema of the kidney without bleeding could also produce such distortion.

A most important piece of information obtained from intravenous urography in the study of a patient with presumed renal injury is the presence and condition of the contralateral kidney. This knowledge is vital if surgical therapy is contemplated for the traumatized kidney with the everpresent possibility of nephrectomy. In addition, intravenous urography has on occasion revealed a pre-existing abnormality of the injured kidney such as tumor, cyst or hydronephrosis. In 59 patients reported by Slade et al.29 6 showed evidence of significant pre-existing disease in the injured kidney and 4 showed important abnormalities in the contralateral kidney. In Hall's10 series of 17 cases, 23 per cent showed unsuspected pre-existing renal disease of the injured kidney. Turton and Williamson³¹ reported 5 cases of injury to a congenital solitary kidney; in 4 of these cases nephrectomy was done.

RETROGRADE PYELOGRAPHY

The use of retrograde pyelography in the study of renal trauma is open to dispute. Some investigators^{18,30} believe that this procedure is contraindicated in such patients in the belief that the study may detach clot and lead to an increase or recurrence of hemorrhage. Another objection to the retrograde study is the possible risk of infecting the injured kidney. Other writers^{8,12,25,26} insist that retrograde pyelography is often necessary for complete evaluation of the traumatized kidney since this method yields best delineation of the

pelvic architecture and is most frequently successful in demonstrating extravasation. Also, the presence of a normal appearing pelvis and calyceal system on retrograde pyelography in the absence of excretion on the intravenous urographic study suggests thrombosis of the renal artery. Tears of the pelvis or ureter are best demonstrated by retrograde study. It thus appears that in the work-up of patients with possible renal injury, if intravenous urography shows absence of excretion on the injured side or excretion so poor that possible tear of the ureter or pelvis could not be diagnosed, careful retrograde pyelography is indicated. Olsson²¹ has suggested that in such instances the retrograde study be done under fluoroscopic control to prevent forcible overdistention of the calyceal system. In addition, of course, retrograde pyelography will reveal other abnormalities that may occur with renal injury such as: filling defects caused by clots, calyceal and pelvic distortion, kidney and ureteral displacement, and extravasation from the calyceal system.

RENAL ANGIOGRAPHY

As already noted, the usual methods of roentgenographic study in patients with suspected renal injury-abdominal roentgenography, intravenous urography and retrograde pyelography-may not disclose the full extent of damage to the kidney. Without more complete information, adequate classification of the degree of injury is not possible, rationale for treatment is in doubt, anticipated course is vague and evaluation of the eventual outcome is inexact. The most valuable and most commonly used study is intravenous urography. However, as emphasized by Olsson and Lunderquist,22 the same urographic changes in the acute stage of renal injury may be present in renal rupture or simply an extrarenal hematoma. It is often impossible to determine from urography whether the kidney has suffered major damage or merely contusion. Several investigators have employed renal angiography in an

effort to discover more exactly the degree of kidney damage. 3,4,6,13,17,22,23,32 Angiography yields accurate information about the state of the blood vessels of the kidney and, in the nephrographic phase, on the condition of the renal parenchyma. The resulting pathologic abnormalities in the kidney are related in large measure to the severity of the initial damage, particularly to damage of the blood supply. Analysis of angiographic abnormalities gives valuable information of the specific abnormality suffered by the injured kidney.

Intrarenal hematoma or edema causes pressure defects on vessels with spreading of the interlobar vessels and their branches generally or locally, depending on the extent of the hematoma. In addition, there may be obliteration of small branch vessels due to the pressure of the hematoma or edema, with lack of the normal vascular arborization in the abnormal region; the consequent lack of normal blood supply leads to a defect in the nephrogram, this defect having unsharp borders as contrasted to the usual sharp borders of a renal cyst.

With extrarenal hematoma there is apt to be displacement of a capsular vessel away from its usual course close to the external surface of the kidney. If large, the extrarenal hematoma deforms the kidney outline by direct pressure and thus causes pressure deformities of vessels in the affected region of the kidney.

If the kidney is ruptured, the fractured segments may be separated from each other or retain a close relationship to each other. Displaced segments generally adhere to major vessels so that the angiogram usually delineates each segment clearly. In the nephrogram phase of the study, there are nonopacified defects due to ischemic areas in the site of rupture.

Thrombosis can occur, as the result of trauma, in the main renal artery or in any of its branches. Block of the main artery or of its major branches is easily shown by angiography. With block of an interlobar vessel, the consequent renal infarct is dem-

onstrated acutely as a localized defect in the nephrogram, best seen in the more intensely opacified renal cortex.

Olsson and Lunderquist²² reported 13 patients with renal trauma studied by renal angiography. In 6 acute cases (within a few weeks of injury), renal rupture was found in 1, perirenal hematoma in 4, and the other patient had a normal angiogram. All 6 patients had abnormal intravenous urograms, none showing extravasation of the contrast medium. Three patients, examined in the subacute stage (a few months following injury), showed no evidence of renal rupture. In 4 patients with old renal injury (few years after trauma), the angiogram showed changes indicating that rupture of the kidney had occurred in 3. In a later paper, Olsson²³ reported the finding of renal rupture in 2 of 15 patients examined by angiography in the acute stage of trauma to the kidney.

Căpek and Fojtîk⁴ described the angiographic findings in 4 children with kidney trauma, all with renal fractures of varying severity. Lamesch¹³ also reported the diagnostic use of angiography in a child with renal rupture.

Maranta and Schnauder¹⁸ indicated that angiography is a crucial study in the evaluation of an injured kidney. They described the angiograms in 6 patients with renal trauma; in 3 a rupture of the kidney was demonstrated and in 1 an occlusion of the main renal artery.

Infarction of the kidney is an uncommon result of trauma. There have been reports of thrombosis of the main renal artery following injury. There have also been reports of traumatic renal infarction where examination of the renal artery disclosed patency of the lumen of the vessel with no evidence of clot; in such cases the infarction was believed to be the result of arteriospasm. If

Traumatic renal arteriovenous fistulas may occur, secondary to penetrating or blunt injury.^{1,28} Such fistulas have also been reported as a complication of percutaneous needle biopsy.^{2,7}

PRESENT STUDY

In most reported cases of the use of angiography in the evaluation of renal trauma, the patients had suffered major injury with urographic evidence of perirenal bleeding or extravasation of the contrast medium. In this study, consecutive cases of renal trauma were examined by renal angiography regardless of the extent of injury. Patients with recognizable catastrophic renal injury were, however, subjected to immediate surgical therapy without angiography. A major aim of this study was to determine whether cases classified as minor renal trauma by the usual methods of examination—abdominal roentgenography and intravenous urography-may show significant vascular changes suggesting abnormalities of a major nature.

There is a preliminary group of 10 patients with renal trauma in whom angiography was not performed and then a group of 24 patients with angiography.

As in other series, most patients were young males—24 (70.6 per cent) were male and 27 (79.4 per cent) were below the age of 31 years (Table 1). Falls and automobile accidents (pedestrian hit by car or passenger in car collision) accounted for the large share of the injuries—21 of 34 (61.8 per cent) (Table 11). In 23 of the 34 patients (67.6 per cent), the left kidney had been injured.

For the purpose of this analysis findings at abdominal roentgenography, intravenous urography or retrograde pyelography (if done) were used to classify each case as minor or serious injury, realizing full well

Table I

34 Patients with renal trauma

Age (yr.)	No. of Patients	
0-10	4	
11-20	16	
21-30	7	
31-40	ϵ	
41-60	0	
61-70	1	

TABLE II

TYPE OF INJURY—34 PATIENTS

Fall	9
Automobile accident (passenger)	6
Hit by automobile	6
Blow in fight	4
Shot or stabbed	4
Football	3
Sledding	1
Percutaneous needle biopsy	1

the possible inaccuracies of the criteria. Any of the following findings led to a classification of serious injury: extravasation of contrast medium, absence of excretion at time of urography, and diminution or obliteration of the kidney outline or of the psoas line in cases in which these features could be definitely evaluated.

In the group of 10 patients without renal angiography, 7 were classified as serious injury; in 3 there was extravasation and in the other 4 there was abnormality of the psoas or renal outline. The remaining 3 patients were classified as minor renal trauma even though they showed positive urographic findings such as diminished contrast medium excretion in general or limited to a localized portion of the calyceal system, distortion of calvces, or presence of a filling defect (clot). In 9 of these 10 patients, the abdominal roentgenogram was made on the day of injury and in the tenth case on the following day. Nine patients were examined by intravenous urography, 7 on the day of injury, I on the next day and the ninth patient on the fifth day following injury.

Twenty-four patients were subjected to renal angiography. The angiogram was negative in 11 patients and positive in 13. In all cases, angiography was accomplished by retrograde catheterization from a femoral artery using the Seldinger percutaneous technique.

NORMAL ANGIOGRAM (11 PATIENTS)

In 1 patient only aortography was done. The other 10 patients underwent both aortography and selective renal angiography. In all 11 patients, the angiographic

Table III
TIME OF ANGIOGRAPHY AFTER INJURY

Time		Positive Angiograms (13 patients)
Within 2 days	4	3
3–7 days	4	2
Within 2 weeks	3	3
Within 3 weeks	-	3
5 weeks		I
II months		I

study was carried out in the acute stage (within a few weeks)—in 8 within the first week of injury and in the other 3 patients within the second week of injury (Table III). Only 2 of these II patients were classified as serious renal trauma—in I the psoas line was obliterated although the urogram was normal; in the other the psoas line was diminished in sharpness and there was extravasation of contrast medium from the renal pelvis. In the patient with obliteration of the psoas line, the retroperitoneal hemorrhage could well have been not from the kidney; the patient had suffered fractures of the ipsilateral transverse process of lumbar vertebrae, I through 4. The other 9 patients with normal angiograms had been classified as having minor renal trauma with normal pyelographic visualization in 7 and diminished visualization in 2. In all patients, abdominal roentgenography and intravenous urography had been carried out in the acute stage of the injury, within a few days of the trauma (Table IV).

POSITIVE ANGIOGRAM (13 PATIENTS)

In 6 patients only aortography was done.

The other 7 patients underwent both aortography and selective renal angiography. In 8 cases the initial angiography was carried out within 2 weeks of the injury, in 3 additional cases within 3 weeks of injury and in the other 2 cases at 5 weeks and 11 months, respectively (Table III). Thus, most of the angiographic studies were done in the acute stage of injury (within a few weeks) and only I (II months) falls in the subacute or chronic stage. Using the classification already mentioned, 12 of the 13 patients were graded as having suffered serious renal injury-4 had absence of excretion of the contrast medium from the injured kidney; 3 showed extravasation of the contrast medium; in 5 patients there was obliteration or diminution in sharpness of the psoas or kidney outline. In this group of 13 patients with positive angiographic findings, only I patient had been classified as suffering from minor renal injury; in this patient the intravenous urogram showed only a diminution in excretion of the contrast medium from the injured kidney. In 12 of the patients, abdominal roentgenography and intravenous urography had been carried out within a few days of the injury, and in the other patient (with an underlying renal neoplasm) at 3 weeks (Table IV).

The major groups of angiographic findings were:

- I. Block of the main renal artery—I case.
- II. Block of a major branch artery (complete or partial)—4 cases.
- III. Non-filling of small peripheral arterial branches—3 cases.

TABLE IV

Time after Injury	Negative Angiograms (11 patients)		Positive Angiograms (13 patients	
	Abdominal Roentgenography	Intravenous Urography	Abdominal Roentgenography	Intravenous Urography
Same day	9	7	9	6
I-4 days	2	3	3	4
5-8 days		Ï	_	2
3 weeks			I	I

- IV. Arteriovenous fistula—2 cases.
- v. Localized displacement of peripheral vessels as the only positive angiographic finding, indicating probable evidence of intrarenal hematoma or edema—I case.
- vi. Underlying malignant renal tumor
 —I case.
- vII. Distortion and diminution in size of vessels—most likely resulting from extensive parenchymal damage—I case.

An analysis of these angiographic findings in relation to other roentgenographic signs as well as clinical data including follow-up studies and findings at operation (if done) may give some indication of the value of angiography in detailing the severity of renal injury as well as the expected prognosis. It appears that if the only angiographic abnormality is displacement of vessels (Group v—probably intrarenal hematoma) the injury to the kidney is minor and the outlook for renal recovery should be good. Similarly, the angiographic finding of lack of small peripheral arterial branches with localized diminution in intensity of the angiographic nephrogram (Group III) appears to carry a good prognosis. The 3 patients in this group seem to have made good recoveries from their renal injury. Very likely, this angiographic finding is related to a laceration of the kidney surface with perirenal hematoma since these 3 patients all showed changes in the psoas or kidney outline (obliteration or diminution in sharpness). In I of these patients at emergency exploratory operation (because of suspected liver injury), a right retroperitoneal hematoma was found; the kidney was not explored and the patient made a good recovery. The other 5 groups carry a more serious prognosis. The I patient with block of the main renal artery (Group 1) underwent nephrectomy 2 days after injury; the kidney was infarcted. In the 4 patients with block of a major branch artery (Group II), I underwent nephrectomy II days following injury, 2 showed abnormal

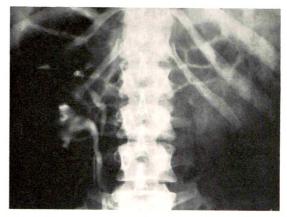


Fig. 1. Case I. No excretion of the contrast medium from the left kidney. Bifid renal pelvis and 2 ureters on the right.

urograms on follow-up study (4 months and 11 months following injury) and the fourth case is not available for follow-up, although his urogram 7 weeks following injury was still abnormal. In the 2 patients with arteriovenous fistula (Group IV), the lesion was discovered during the investigation of hematuria following trauma and was proved at subsequent nephrectomy. The 1 patient in Group VII with proven rupture of the kidney and residual positive angiogram continues to show an abnormal urogram 19 months following the injury.

CASES WITH POSITIVE ANGIOGRAM

GROUP I. BLOCK OF THE MAIN RENAL ARTERY

CASE I. R.A., a 17 year old girl, was admitted to the hospital on February 13, 1964 one hour after having been struck by a truck. She had pain in the left chest and left flank. Blood pressure was 120/80 and hematocrit 39. No abdominal masses were palpable. There was microscopic hematuria. An immediate abdominal roentgenogram showed no free air, no fractures and no scoliosis; because of gas and fecal matter in the intestinal tract, the psoas muscle and renal outlines could not be seen on either side. On the next day, an intravenous urogram demonstrated no excretion of contrast medium from the left kidney (Fig. 1); a left retrograde pyelogram made after the intravenous urography showed a normal calyceal system (Fig. 2). An aortogram on the second day following injury demonstrated a clot in the left renal artery causing almost complete block of the artery (Fig. 3).

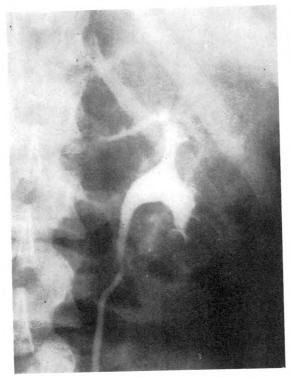


Fig. 2. Case 1. Normal left retrograde pyelogram.

Operation immediately after the aortography disclosed infarction of the left kidney with scattered areas of black and hemorrhagic discoloration. A clot was found in the renal artery with lack of arterial pulsations distal to the clot. The clot was removed by arteriotomy with reestablishment of blood flow through the renal artery; however, the appearance of the kidney did not improve and nephrectomy was done. There was a moderate amount of blood in the retroperitoneal space. Pathologic study confirmed the diagnosis of renal infarction.

Comment. The operation was done immediately after angiographic demonstration of the clot, but this was already 48 hours after the injury. Possibly earlier aortography followed by earlier surgery might have allowed survival of the kidney.

GROUP II. BLOCK OF A MAJOR BRANCH ARTERY

CASE II. V. M., a 23 year old man, was admitted to the hospital on June 26, 1964 shortly after having been struck by a truck. He had multiple rib fractures on the left, a left tension pneumothorax, fracture of the left transverse process of L-4, and microscopic hematuria. On

admission, pulse was 130 and blood pressure 90/0. An abdominal roentgenogram showed neither psoas nor renal outline clearly. There was no lumbar scoliosis. Abdominal taps were positive for blood. After therapy for the pneumothorax, immediate laparotomy disclosed two liters of blood in the peritoneal cavity; the spleen was ruptured into 3 separate fragments. There were also serosal tears of the transverse colon and of the proximal jejunum as well as a 2 cm. laceration of the liver. The spleen was removed, the intestinal tears were sutured and the liver laceration was packed with gelfoam. There was a hematoma in Gerota's fascia on the left; this was opened to expose the kidney which was smooth in contour with no evidence of capsular tear. The right kidney appeared normal.

An intravenous urogram 7 days after the injury (Fig. 4) revealed poor excretion of the contrast medium on the left with very poor visualization of the mid and lower calyces. Early films showed no excretory nephrogram and the later films showed hypoconcentration of the contrast medium in a poorly filled calyceal system (appearance of low output kidney). No extravasation of the contrast medium could be visualized. The right kidney appeared nor-

On the thirteenth day after the accident aortography and left selective renal angiography were performed (Fig. 5, A-D). There was narrowing of the dorsal artery a few millimeters from its origin with slow flow in its branches

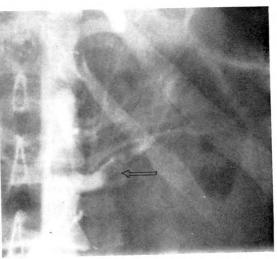


Fig. 3. Case i. Aortogram shows clot in the left renal artery (arrow).

and marked diminution in the nephrogram intensity of the posterior portion of the kidney, best seen in the lateral selective study. In the anteroposterior projection there was loss of cortical intensification at the medial aspect of the kidney. The angiogram of the right kidney appeared normal; there were 2 renal arteries on the right. The kidneys were about equal in length (the left about 3 mm. shorter).

Three months after injury, intravenous urography still showed the appearance of a low output kidney on the left; the upper calyces still visualized better than the mid and lower groups. Both psoas outlines were well defined.

Four months following the accident a repeat left selective renal angiogram still showed narrowing of the dorsal artery, lack of cortical intensification at the medial aspect of the kidney in the nephrogram phase on the anteroposterior projection, and diminished nephrogram intensity of the posterior portion of the kidney in the lateral projection (Fig. 6, A and B). Both kidneys were still about the same size in length (the left about 7 mm. shorter). Blood pressure was normal, 120/80. At this time there was no hematuria.

Comment. There is little doubt that this is an instance of primary vascular damage to the dorsal renal artery due to trauma. At exploratory laparotomy on the day of injury, the kidney appeared smooth with no evidence of laceration or rupture. Initial angiography was done 13 days after injury and it is unlikely that arteriospasm would still be present this long after injury. Furthermore, the changes were still present at the repeat angiography 4 months following injury. The seriousness of damage to the kidney was not apparent on intravenous urography and could be appreciated only on angiography.

Case III. W. G., an II year old boy, was struck by an automobile on November 21, 1961 and was admitted to the hospital with evidence of intra-abdominal bleeding. Immediate laparotomy disclosed a ruptured spleen; splenectomy was performed. At operation, a left perinephric hematoma was seen but not explored because there had been no preoperative hematuria. He did well postoperatively until the sixth day when he developed hematuria which lasted IO days and stopped spontaneously. An intravenous



Fig. 4. Case II. Five minute roentgenogram during intravenous urography. Diminished pyelogram on the left, especially of the mid and inferior calyceal groups.

urogram 5 days after the accident showed poor excretion of the contrast medium on the left, intrarenal extravasation of the medium in the midportion of the kidney, slight lateral displacement of the left kidney and obliteration of the left psoas line. The right kidney appeared normal. A repeat intravenous urogram 9 days after the accident showed the same findings (Fig. 7).

An intravenous urogram 8 months after the accident showed the left kidney to be small with excretion only from the lower group of calyces; there was no extravasation. Eleven months following injury, an intravenous urogram (Fig. 8) again showed excretion of contrast medium only from the lower calyces on the left and the left kidney was even smaller than at the study 3 months previously. The right kidney appeared normal. The left psoas muscle was well defined.

An aortogram 11 months after the accident (Fig. 9) showed 3 renal arteries on the right. On the left a single renal artery of normal diameter at its origin tapered to a small lumen with only a few thin branches supplying the lower part of the left kidney. The left kidney showed a nephrogram only of its lower part. Blood pressure was normal, 118/65.

Comment. The aortogram showed the left main renal artery to continue directly into the kidney apparently as the ventral artery with absence of the dorsal artery. There was a small irregularity at the superior sur-

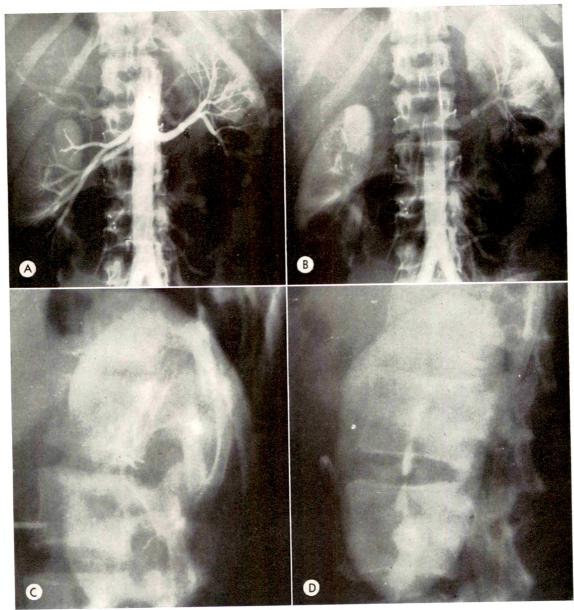
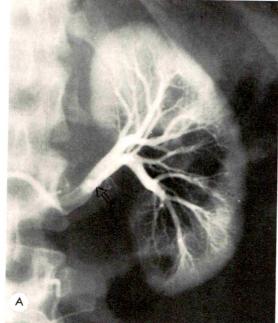


Fig. 5. Case II. (A) Aortogram shows irregularity of the dorsal renal artery on the left. (B) Aortogram, 0.25 second after A, shows diminished cortical intensification at the medial aspect of the left kidney. The renal arteries on the left remain opacified longer than those on the right. (C) Selective left renal angiogram, lateral projection, shows poor opacification of the posterior part of the kidney during the nephrogram phase. (D) Lateral view of a normal kidney during the nephrogram phase of a selective renal angiogram to demonstrate the usual homogeneous opacification, Compare this with C.

face of the main renal artery at the expected site of bifurcation, suggesting the possibility of an orifice of an occluded dorsal artery. It is on the basis of lack of branching of the main renal artery that the presumptive diagnosis of traumatic occlusion of the dorsal artery was entertained. The possibility cannot be completely excluded that the vascular change is secondary to primary parenchymal damage to the kidney and that this case belongs more properly in Group VII, although it is more



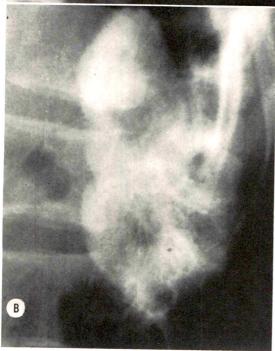


Fig. 6. Case II. (A) Four months after injury, selective angiogram still shows irregular narrowing of the dorsal artery near its origin as well as diminished cortical intensification at the medial aspect of the kidney. (B) Four months after injury, lateral projection of the selective angiogram still shows irregular and diminished nephrogram intensity of the posterior portion of the kidney.

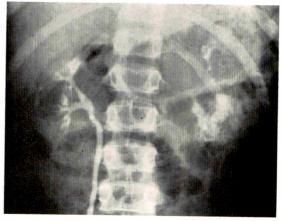


Fig. 7. Case III. Intravenous urogram showing extravasation from the left mid-calyceal group.

likely that there was primary vascular damage.

Case IV. M. B., a $2\frac{1}{2}$ year old boy, was in good health until he fell from a window on the third floor to a concrete pavement, suffering an occipital skull fracture on July 20, 1964. He was admitted to the hospital soon after the fall, alert and crying. Blood pressure was 120/70. There was no hematuria. Four days after the accident his blood pressure rose to 150/100; all previous levels since injury had been 110 to 130 systolic and 60 to 70 diastolic. An intravenous urogram at this time (4 days after injury) showed no excretion of contrast medium from the left kidney; the right kidney appeared normal. Aortograms on the next day (5 days after the fall) showed both renal arteries to appear normal at their origin (Fig. 10, A, B and C). The left renal artery became irregularly narrowed about I cm. from its origin with no filling of the



Fig. 8. Case III. Eleven months after injury, the intravenous urogram shows excretion of the contrast medium only from the lower calyceal group.

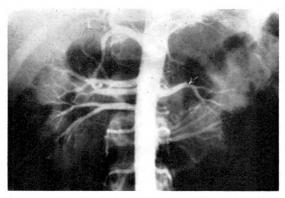


Fig. 9. Case III. Aortogram II months after injury shows lack of arterial branches to the left kidney. The irregularity at the superior surface of the left main renal artery (arrow) may represent the orifice of an occluded dorsal artery.

dorsal renal artery. The remaining intrarenal arteries on the left, branches of the ventral artery, showed slow flow of the opacified blood and there was not a good nephrogram. The left kidney was small. The angiogram of the right kidney appeared normal.

A repeat intravenous urogram on the ninth day following injury still showed no excretion of contrast medium by the left kidney. The patient was on antihypertensive medication but the blood pressure was still elevated, 140/90. Urinalysis showed o to few red blood cells per high power field.

On the eleventh day following trauma, left nephrectomy was done. At operation, the left renal artery showed diminished pulsations and the kidney appeared small and anemic. There was no perinephric hematoma and the renal capsule appeared intact. The renal vein was normal in size. Two months postoperatively blood pressure was 120 to 130 systolic and 70 to 80 diastolic.

Pathologic study of the kidney showed large areas of acute infarction. The cortical surface was smooth with no evidence of rupture. The pelvis and calyces appeared normal.

Comment. It is presumed that the changes of the left kidney were related to the trauma, due to injury to the wall of the left main renal artery with thrombosis of the dorsal renal artery. Previous abnormality of this kidney cannot be completely excluded, such as congenital hypoplasia. However, the normal size of the left renal

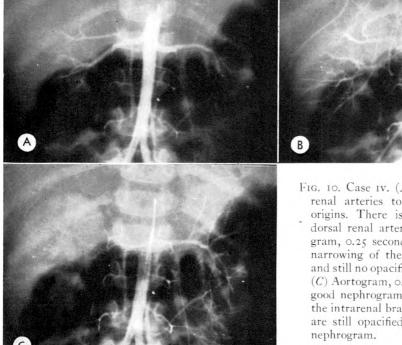


Fig. 10. Case IV. (A) Aortogram shows both renal arteries to appear normal at their origins. There is no opacification of the dorsal renal artery on the left. (B) Aortogram, 0.25 second after A, shows irregular narrowing of the left renal artery (arrow) and still no opacification of the dorsal artery. (C) Aortogram, 0.50 second after B, shows a good nephrogram on the right. On the left the intrarenal branches of the ventral artery are still opacified and there is hardly any

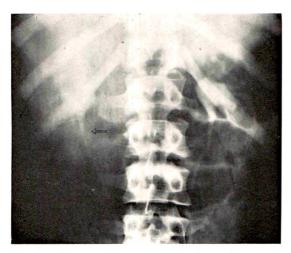


Fig. 11. Case v. Intravenous urogram shows poor excretion on the right with suggestive intrarenal extravasation of the contrast medium. The upper right ureter is displaced laterally (arrow) and the right psoas line is obliterated.

artery at its origin with the abrupt change about I cm. from its origin and the paucity of its branches with slow flow in the existing branches suggest that the abnormalities were due to injury. Also, pathologic study of the removed kidney demonstrated acute infarction.

CASE v. C. S., a 19 year old male, was stabbed in the right flank on May 30, 1964. He was admitted to the hospital in shock. There was gross hematuria. After multiple blood transfusions the blood pressure rose to 110/70; an intravenous urogram showed diminished excretion of the contrast medium from the right kidney with no well defined calvceal system outlined (Fig. 11). An irregular collection of the contrast medium in the kidney suggested intrarenal extravasation. The right psoas line was obliterated and there was lateral displacement of the right kidney and upper right ureter. The left kidney appeared normal. An immediate right retrograde pyelogram demonstrated extravasation of contrast medium into the renal parenchyma medially from the upper group of calyces. Operation disclosed a laceration about 3 cm. long in the posterior aspect of the right kidney close to the hilus with no demonstrable injury to the renal pelvis or renal pedicle. There was a large amount of blood in the perinephric space. No intraperitoneal blood was noted. Mattress sutures were passed through the area of the kidney laceration and tied over surgicel.

Postoperatively, the patient drained urine through the drain placed near the kidney, this drainage persisting for about 2 weeks. The urine drainage was thought to be due to a calyceal tear.

On the twelfth day following injury a right selective renal angiogram showed block of a major branch of the dorsal renal artery close to the hilus (the branch going to the lower pole), with diminution in the nephrogram of the lower pole medially and posteriorly (Fig. 12). Preliminary aortography had shown the presence of a single right renal artery with no separate polar vessels.

Follow-up intravenous urograms (18 days and 7 weeks following the injury) disclosed an increasing right hydronephrosis with delayed emptying of the dilated pelvis and deformity of the medial aspect of the renal pelvis. The right kidney and ureter had returned to their normal position. Unfortunately, the patient has not been available for further follow-up studies.

Comment. It is difficult to determine whether the vascular change is due to the trauma of the original stab wound or due to the surgery. It is quite possible that the vascular block was caused by the suture applied at operative therapy for the kidney laceration.

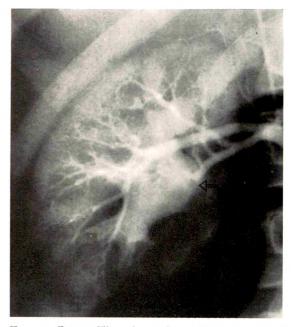


Fig. 12. Case v. There is an abrupt block (arrow) of a major arterial branch to the lower pole.

GROUP III, NON-FILLING OF SMALL PERIPHERAL ARTERIAL BRANCHES

Case vi. R. S., an 8 year old boy, fell from a swing on September 20, 1964. The injury consisted of a fall of about 10 feet, striking his abdomen on a rock. He was immediately brought to the hospital complaining of abdominal pain. Blood pressure was 114/60. No abdominal masses could be felt; there was tenderness and rigidity in the left kidney area. There was gross hematuria. Abdominal tap was negative for blood. An immediate intravenous urogram showed diminished excretion and hypoconcentration of contrast medium on the left with no evidence of extravasation of the medium (Fig. 13). There was loss of clarity of the upper psoas line and of the outline of the upper pole of the left kidney.

Gross hematuria cleared within a few days although microscopic hematuria persisted for 8 days.

On the day following injury an aortogram (Fig. 14) showed 2 renal arteries on the left and I on the right, all appearing normal. The intrarenal arteries on the right appeared normal. In the left kidney there were abnormalities of several small vessels in the upper pole; they seemed stripped of their arborizing branches as compared to vessels of similar size in other portions of the kidney. Also, the nephrogram was of diminished intensity at the upper pole on the left. The kidneys were about equal in size.

At follow-up clinic visit 3 months after injury, the patient felt well; blood pressure was 100/60. An intravenous urogram 6 months fol-



Fig. 13. Case vi. Intravenous urogram shows poor excretion on the left and diminution in clarity of the left psoas line.

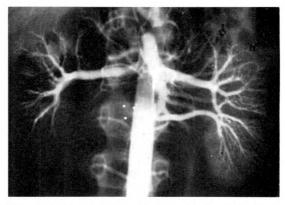


Fig. 14. Case vi. Aortogram shows lack of opacification of the small peripheral branches at the upper pole (arrows) of the left kidney.

lowing injury appeared normal with the kidneys normal in size.

Comment. The initial urographic changes allowed no true evaluation of the extent of renal damage since patients with damage to a major branch artery could show a urogram no more abnormal than here (e.g., Case II). However, the angiogram indicated minor vascular changes.

CASE VII. D. H., a 17 year old male, was admitted to the hospital on December 19, 1964 because of left upper quadrant pain and gross hematuria following blunt trauma to the abdomen while playing football. Blood pressure was 130/70. An immediate abdominal roentgenogram showed obliteration of the left psoas line and slight scoliosis of the lumbar spine concave to the left. There were no fractures of the spine or the ribs. An intravenous urogram showed diminished excretion of the contrast medium on the left with a poor excretory nephrogram on the I minute film and hypoconcentration of the medium in the pyelographic phase. There was distortion of the lower group of calyces. There was no extravasation of contrast medium (Fig. 15).

Hematuria, at first gross and later microscopic, continued for 10 days. Aortography and selective left renal angiography on the second day following trauma showed a large renal cyst at the lateral aspect of the left kidney. In addition, there was poor filling of the small vessels at the lower pole of the kidney with less cortical intensification and a poor nephrogram at the

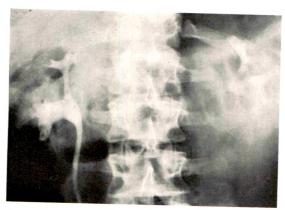


Fig. 15. Case vii. Intravenous urogram shows diminished excretion of the contrast medium on the left.

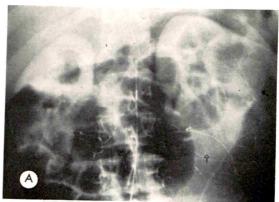
lower pole, especially at its medial aspect (Fig. 16, A and B).

Comment. In spite of its large size, the renal cyst was not recognizable on the initial intravenous urogram at which time there was poor excretion of the contrast medium on the left. In addition to disclosing the pre-existing lesion, the angiogram demonstrated minimal vascular changes indicating no severe parenchymal damage to the kidney. With conservative treatment the patient followed a benign clinical course and left the hospital after 11 days. Two months later, he is normotensive and doing well.

Case vIII. R. L., a 15 year old boy, was thrown to the pavement from his bicycle when he hit a parked automobile on July 21, 1964. He was admitted to the hospital soon after the accident because of right flank pain and gross hematuria. Blood pressure was 100/60. There was tenderness in the right flank; no abdominal masses could be felt. Hematocrit was 35. An immediate abdominal roentgenogram showed diminution in sharpness of the right psoas line. An intravenous urogram on the day of injury showed excretion of the contrast medium bilaterally with no evidence of extravasation. Because of suspected liver injury, an exploratory laparotomy was done on the day of hospital admission; the intraperitoneal structures were found to be intact. A large retroperitoneal hematoma was noted on the right side but this area was not explored.

Aortograms, 3 weeks after injury, showed a separate upper pole artery to each kidney. The segmental artery to the lower pole on the right appeared abnormal with lack of fine arterial branching. There was irregular diminution in the intensity of the nephrogram at the lower pole. The right kidney was smaller than the left (Fig. 17, \mathcal{A} and \mathcal{B}).

Follow-up intravenous urography 7 months after the injury showed good excretion of the contrast medium bilaterally. The right kidney measured about 2 cm. less in length than the left kidney—the same disparity as noted at aortography 3 weeks following the injury.



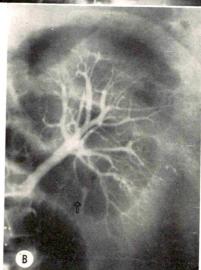
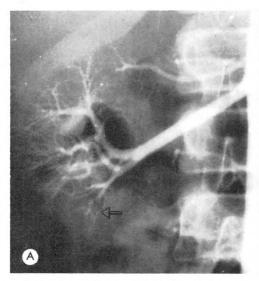


Fig. 16. Case VII. (A) Aortogram, nephrogram phase, shows a large renal cyst at the lateral aspect of the left kidney (upper arrow). There is diminution of the nephrogram intensity at the lower pole medially (lower arrow). (B) Selective renal angiogram shows poor filling of the peripheral vessels at the lower pole medially (arrow).



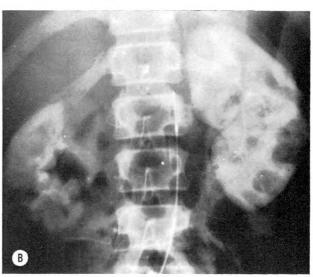


Fig. 17. Case VIII. (A) Aortogram shows a separate upper polar artery. There is irregular opacification of interlobar arteries at the lower pole (arrow) with lack of opacification of the finer peripheral branches. (B) Aortogram, nephrogram phase, shows diminution in intensity of the nephrogram at the lower pole on the right. The lessened nephrogram intensity at the upper pole is most likely due to layering of the contrast medium in relation to the orifice of the polar artery, resulting in a lower concentration of the contrast medium to the polar vessel.

Repeat aortography and selective right renal angiography 7 months following the trauma still showed abnormality of the branches of the lower pole vessels of the right kidney. There were several small branches extending beyond the renal outline at the lower pole, possibly representing vessels into an organized hematoma related to previous laceration of the kidney. In addition, the lower pole of the right kidney appeared flattened (Fig. 18).

Comment. The angiographic abnormalities 3 weeks after the accident were slight, in spite of which the angiogram still showed minor changes 7 months following the injury. However, the urogram showed no major positive findings 7 months after the trauma. The significance of the difference in kidney size is difficult to evaluate—whether it represents a pre-existing abnormality or actually is a result of the injury. Clinically, the patient has done well, with normal blood pressure.

GROUP IV. ARTERIOVENOUS FISTULA

CASE IX. R. S., a 17 year old male, was stabbed in the left upper quadrant on May 17, 1964, shortly before admission to the hospital

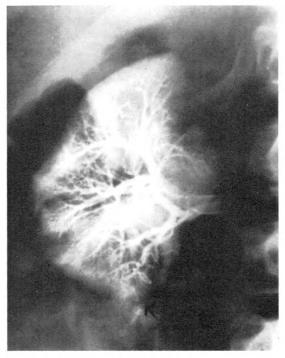


Fig. 18. Case viii. Selective angiogram, 7 months after injury, shows several small arterial branches extending beyond the renal outline (arrow). The lack of opacification of the upper pole is due to the presence of an upper polar artery, not catheterized.



Fig. 19. Case IX. Intravenous urogram shows poor excretion of the contrast medium by the left kidney. There is a filling defect in the renal pelvis due to blood clot.

in shock and with gross hematuria. After blood transfusions with restitution of blood pressure to 120/60, intravenous urography showed poor excretion of the contrast medium on the left with evidence of a blood clot in the left renal pelvis and bladder. The opacification of the left calyceal system was not good enough to evaluate the possibility of extravasation. The upper left ureter was displaced laterally, apparently by a retroperitoneal hematoma (Fig. 19). A left retrograde pyelogram made right after the intravenous urogram showed irregularity of the superior infundibulum with extravasation of a small amount of contrast medium from a superior calyx (Fig. 20). Immediate exploratory laparotomy revealed about 2 liters of blood and clots in the peritoneal cavity, laceration of the left transverse colon and bleeding from the anterior surface of the left kidney. The laceration of the midportion of the left kidney did not appear to penetrate to the posterior surface and at surgery the laceration was not seen to involve the calyceal system or renal pelvis. The colon wound was sutured. No sutures were taken in the kidney; the bleeding was stopped readily with tamponade.

Postoperatively, the patient continued to have gross hematuria for 13 days. Then after 2 days of clear urine grossly, massive hematuria recurred, necessitating transfusion.

On the seventh day after injury, intravenous urography showed poor excretion of the contrast medium on the left, lateral displacement of the upper portion of the left ureter and diminution in sharpness of the left psoas line. No extravasation could be seen.

Aortography and selective left renal angiography on the eighteenth day after trauma, during the recurrent gross hematuria, showed a large arteriovenous fistula in the upper part of the left kidney with early opacification of several large veins (Fig. 21, A and B). On the next day left nephrectomy was done. Pathologic examination demonstrated the fistula.

Comment. The retrograde pyelogram demonstrated a break in the calyceal system (extravasation) not shown by the intravenous urogram. Yet the most serious damage, the arteriovenous fistula, was not suspected after the regular roentgenographic studies and not even at the time of direct inspection of the kidney during the emergency laparotomy. The angiogram is the definitive study for this abnormality.



Fig. 20. Case IX. Retrograde pyelogram shows extravasation from a superior calyx.

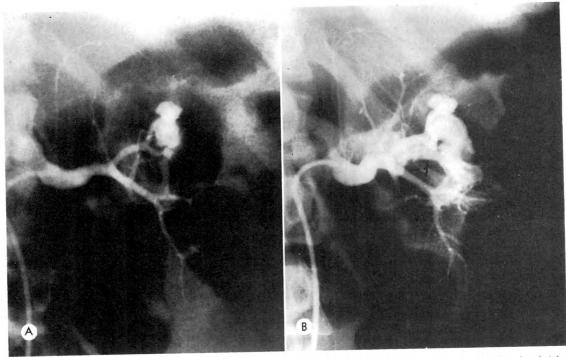


Fig. 21. Case IX. (A) Selective angiogram shows early pooling of the contrast medium in the fistula, fed by an upper interlobar artery. (B) Selective angiogram, later film, shows early opacification of intrarenal veins (closed arrow) and of the main renal vein (open arrow) through the arteriovenous fistula.

CASE X. R. G., a 10 year old girl with glomerulonephritis, underwent a percutaneous needle biopsy of the right kidney on May 27, 1964. The kidney was punctured twice. After biopsy there was gross hematuria and right flank tenderness. Gross hematuria and clots continued for 4 days and the urine then cleared. Eight days after the biopsy, gross hematuria recurred with evidence of falling hematocrit.

On the day following biopsy, an abdominal roentgenogram showed diminution in sharpness of the right psoas line, partial obliteration of the right renal outline and scoliosis of the lumbar spine, concave to the right.

An intravenous urogram 2 days following biopsy demonstrated a large right kidney and poor excretion on the right, especially from the lower calyces, and attenuated infundibula. The right psoas line was obliterated. The appearance suggested intrarenal and extrarenal hematoma. However, no extravasation of the contrast medium was seen (Fig. 22). A repeat intravenous urogram 8 days postbiopsy, during the recurrence of gross hematuria, showed absence of excretion of the contrast medium on the right.

Aortography and selective right renal angiog-

raphy on the tenth day following biopsy showed streching of the intrarenal vessels on the right and puddling of the contrast medium at the lower pole of the kidney with rapid opacification of veins. (Fig. 23, A and B). Following angiography, the enlarged right kidney showed the appearance of an obstructive nephrogram (Fig. 24). On the following day right nephrec-

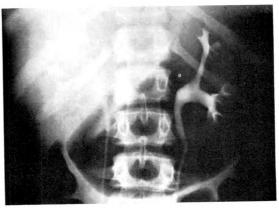


Fig. 22. Case x. Intravenous urogram shows the right kidney to be large with poor excretion of the contrast medium.

tomy was done. Pathologic study demonstrated the arteriovenous fistula. The kidney was generally enlarged, firm and diffusely hemorrhagic. There was an organized hematoma completely surrounding the kidney beneath Gerota's fascia as well as around the renal pedicle and upper ureter. The renal pelvis was distended with clot. Two lacerations were noted on the kidney surface.

Comment. Arteriovenous fistula formation is a recognized complication of percutaneous needle biopsy of the kidney. In the absence of routine postbiopsy angiography, the true incidence of this complication cannot be estimated. Only the large fistulae and those associated with continued intrarenal and extrarenal bleeding come to further study and diagnosis. The obstructive nephrogram immediately following angiography was apparently related to the large blood clot in the renal pelvis, causing obstruction to the emptying of the calyceal system.

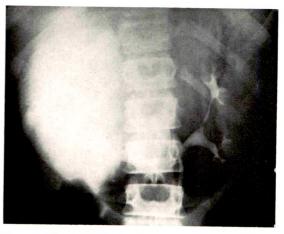


Fig. 24. Case x. Roentgenogram 60 minutes following angiography shows an obstructive nephrogram on the right.

GROUP V. LOCALIZED DISPLACEMENT OF PERIPHERAL VESSELS

Case xi. C. V., a 24 year old woman, was admitted to the hospital on July 14, 1964 because of 3 days of gross hematuria following a

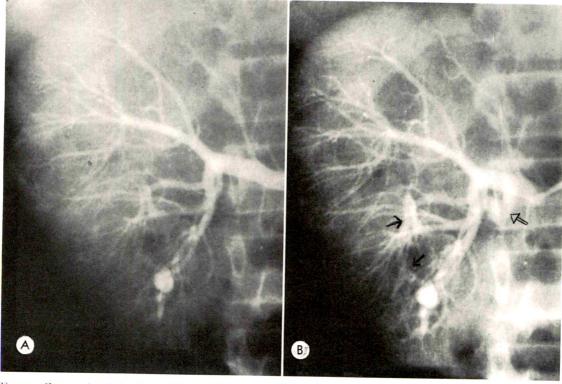


Fig. 23. Case x. (A) Selective angiogram shows pooling of the contrast medium in the fistula, fed by a lower interlobar artery. (B) Selective angiogram, later film, shows early opacification of intrarenal veins (closed arrows) and of the main renal vein (open arrow).

27/590

hard blow to the left flank. Blood pressure was 110/80. There was left flank tenderness but no abdominal masses could be felt. She denied previous urinary symptoms.

Intravenous urography on the day of admission showed evidence of atrophic chronic pyelonephritis on the right with compensatory hypertrophy of the left kidney. There was poor excretion of the contrast medium from the left kidney.

Hematuria, at first gross and later microscopic, continued for 4 days after hospitalization. Aortography and selective left renal angiography, 5 days after injury, showed minimal downward displacement of two branches of the ventral artery with no disturbance of the nephrogram or of cortical intensification (Fig. 25). These slight angiographic abnormalities were considered due to a small intrarenal hema-

Comment. This patient had a benign clinical course with disappearance of all symptoms within a few days. She was hos-

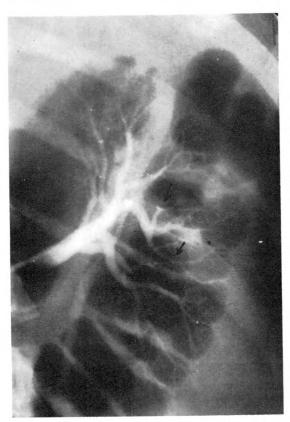


Fig. 25. Case XI. Selective angiogram shows slight displacement of interlobar arteries (arrows).

pitalized for only 4 days. At follow-up study I month later she was asymptomatic; blood pressure was 110/70. The angiographic changes were minimal, representing at most slight vascular distortion from a small intrarenal hematoma or edema.

GROUP VI. UNDERLYING MALIGNANT RENAL

CASE XII. F. R., a 19 year old woman, noted back pain and hematuria following a fight with her husband during which she received a hard kick in the back. She was admitted to the hospital 3 weeks after the injury because of persistence of pain and gross hematuria. Four years previously during her first pregnancy she was told that she had right sided pyelonephritis.

There was marked right flank tenderness. Blood pressure was 130/80 and the hematocrit 14. An immediate abdominal roentgenogram showed no fractures but there was scoliosis of the lumbar spine, concave to the right. Psoas and renal outlines could not be seen on either side. An intravenous urogram demonstrated no excretion of contrast medium on the right with good excretion from the left kidney. There was a large filling defect in the bladder, presumably representing a large blood clot (Fig. 26). Immediate aortography and selective right renal angiography disclosed a large mass occupying the upper portion of the right kidney. The presence of abnormal vessels led to the roentgenologic diagnosis of malignant tumor (Fig. 27). Right nephrectomy demonstrated a large fibrosarcoma involving the right kidney with extension into the renal pelvis and forming a tumor cast of the lower calyces. Several months later the patient died of metastatic disease.

Comment. An important advantage of diagnostic study of patients with suspected kidney injury is the uncovering of pre-existing renal lesions. In this patient the presumptive clinical diagnosis after physical examination, abdominal roentgenography and intravenous urography was "large hematoma of the right kidney due to injury." The angiographic findings led to the correct preoperative diagnosis. The lack of excretion of the contrast medium at the time of intravenous urography was due to the filling of the calyceal system by neoplasm.



Fig. 26. Case XII. Intravenous urogram shows no excretion of contrast medium by the right kidney. The large oval filling defect in the bladder represents blood clot. The smaller bladder filling defect is due to the Foley catheter.

GROUP VII. DISTORTION AND DIMINUTION IN SIZE
OF VESSELS RESULTING FROM PARENCHYMAL
DAMAGE

Case XIII. N. G., a 7 year old girl, fell from a second story window on July 16, 1963, suffering bilateral Colles' fractures and fracture of the pelvis. She was admitted to the hospital in shock. There was gross hematuria. An intravenous urogram showed no excretion of contrast medium on the right. The right psoas line was obliterated (Fig. 28). A right retrograde pyelogram demonstrated extravasation of opaque medium from the upper group of calyces into the perirenal space (Fig. 29).

On the third day following injury, operation disclosed a fracture of the upper pole of the right kidney. A large subcapsular hematoma was drained; no kidney tissue was removed. Microscopic hematuria continued for several weeks.

Postoperatively, she had episodes of hyper-

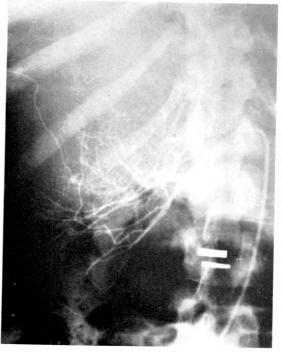


Fig. 27. Case XII. Selective angiogram shows a large renal neoplasm with multiple tumor vessels.

tension with blood pressure elevated to levels of 148 to 162 systolic and 88 to 90 diastolic. Several repeat intravenous urograms showed poor excretion of contrast medium by the right kidney.

Five weeks following injury, aortograms showed the left renal artery and its branches to appear normal. The right renal artery appeared



Fig. 28. Case XIII. Intravenous urogram shows no excretion of the contrast medium by the right kidney. The right psoas line is obliterated.



Fig. 29. Case XIII. Retrograde pyelogram shows extravasation from the upper calyces.

normal at its origin, but it quickly tapered to a narrow lumen with crowded branches in a small right kidney. There was loss of nephrogram in-

tensity of the upper portion of the right kidney (Fig. 30, A and B).

Follow-up intravenous urograms, 16 and 19 months following injury, showed the small right kidney with markedly thinned upper cortex and a poor excretory nephrogram in its upper portion. Early films of the urographic studies demonstrated diminution of excretion into the upper calyces. Blood pressure 19 months after the accident is normal, 90/60.

Comment. The vascular changes here are most likely secondary to injury to the parenchyma of the kidney with marked post-traumatic renal atrophy. Fracture of the upper portion of the kidney had been demonstrated at operation 3 days following the injury.

DISCUSSION

There is no completely satisfactory method of classifying the severity of renal injury short of examination of the kidney at autopsy or after nephrectomy.

A most informative roentgenologic study in this respect is intravenous urography although there are severe limitations to this examination. Break in the calyceal system or tears in the pelvis or ureter may not be demonstrated by intravenous urography, especially when there is diminution in the

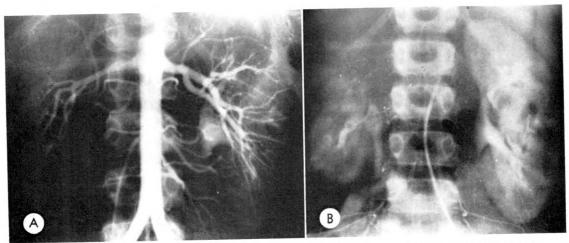


Fig. 30. Case XIII. (A) Aortogram shows the narrowed right renal artery. The intrarenal arterial branches are crowded with no opacification of the finer peripheral branches. (B) Aortogram, later film, shows an irregular nephrogram on the right, generally diminished in intensity. There is no observable nephrogram of the upper pole of the small right kidney.

excretion of the contrast medium by the injured kidney. In cases where the visualization of the calyceal system is poor at the time of intravenous urography, careful retrograde pyelography is probably indicated to eliminate the possibility of extravasation.

Renal angiography can add important information in the evaluation of a patient with suspected kidney injury. The procedure carries relatively little risk. Several previous reports conclusively demonstrate the great value of angiography in diagnosing renal rupture. However, trauma to the kidney may produce primary damage to the blood vessels of the kidney and it is in this type of injury that angiography alone can yield significant diagnostic data, not available from intravenous urography or retrograde pyelography.

SUMMARY

Twenty-four patients with suspected renal trauma have been studied by renal angiography. Each patient was initially classified as having suffered minor or serious kidney injury based on findings at abdominal roentgenography, intravenous urography and retrograde pyelography (if done). Any of the following findings classified a case as one of serious injury: extravasation of contrast medium, absence of excretion at time of intravenous urography, and diminution or obliteration of kidney outline or of the psoas line where these features could be evaluated.

Ten of the 24 patients were classified as cases of minor injury; 9 showed normal angiograms and the other patient's angiogram demonstrated minimal or debatable changes of no great consequence. Fourteen cases were initially classified as serious kidney injury; 12 of these had positive angiograms. Thus, renal angiography need not be part of the diagnostic work-up of all patients with suspected renal injury, but only in those classified as "serious injury" as described here.

The major angiographic findings were: thrombosis of the main renal artery; block

of a major branch artery; non-filling of small peripheral arterial branches; arteriovenous fistula; localized displacement of peripheral vessels; underlying major renal disease; and vascular changes due to parenchymal damage after renal rupture. The relative significance of these findings in respect to the severity of kidney damage has been exemplified in the case reports.

Emphasis is placed on the occurrence of vascular thrombosis and arteriovenous fistula resulting from renal trauma and on the important contribution of renal angiography to the proper evaluation of such patients.

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SPONTANEOUS RENAL EXTRAVASATION DURING INTRAVENOUS UROGRAPHY*

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INTRAVENOUS urography performed during or immediately after an acute urinary stone colic attack usually shows an enlarged "white" kidney (obstructive nephrogram) with a delayed urogram (obstructive pyelogram)^{5,8} on the affected side. In rare cases, however, this examination yields a different picture, consisting of the appearance of contrast material outside the collecting system of the kidney, either intrarenally or extrarenally, in the retroperitoneal tissue. This finding is usually noted without the appearance of a "white" kidney, but is sometimes associated with increased opacification of the affected kidney. Such an extravasation of contrast material from the collecting system of the kidney is a well recognized occurrence on retrograde pyelography8,18,80 but has been described on intravenous urography in only a few reports. The first such report came in 1930 from Fuchs,12 and others have appeared sporadically since then. 4,6,9,11,13,15,16,19,21,22,26 The purpose of the authors is to report 16 cases of spontaneous extravasation seen on intravenous urography and to record some features not hitherto described.

DEFINITION

Before proceeding to deal further with the subject of spontaneous extravasation of contrast material, we feel that it is essential to define clearly what is meant by the terms, "spontaneous" and "extravasation," particularly since there appears to be some confusion in the literature about them.

For the occurrence to be classified as "spontaneous," the following criteria must be fulfilled:

- I. Absence of recent ureteric instrumentation. Ureteric catheterization or retrograde pyelography may give rise to perforation or rupture of a calyceal fornix. This may remain open, or be easily reproduced, for several weeks, especially if it has occurred in a kidney which is the site of disease, such as tuberculosis or chronic pyelonephritis. We have seen such extravasation on repeat retrograde examination with very low pressure filling, 3 weeks after a prior rupture; therefore, any cases with a history of such instrumentation during the previous 3 weeks are excluded from consideration in this series.
- 2. Absence of previous surgery. Such previous surgery on the kidney or upper ureter, or in the immediate vicinity, may result in a fistulous communication between the collecting system and the retroperitoneal space, and intravenous urography performed in such cases may show contrast material outside the collecting system.
- 3. Absence of external trauma. External trauma may cause a similar condition to that stated above^{1,6,29} and cases with such a history are, therefore, excluded from consideration.
- 4. Absence of a destructive kidney lesion. In the presence of a neoplastic or other destructive process in the kidney, the contrast material may collect in irregular small cavities or channels outside the pelvicalyceal system, and give a picture very similar to that seen in extravasation. In addition, it is well recognized that true, spontaneous extravasation of urine or contrast material may occur in the presence of such disease, and may amount even to spontaneous rupture of the kidney. In such cases, especially when the first examination has been

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performed during an acute episode such as a clot colic, one or more repeat roentgenologic examinations, after the acute phase, may be necessary to establish the correct diagnosis.

5. Absence of external compression. It has been shown that external ureteral compression applied during intravenous urography results in extravasation, sometimes extensive, in about 2 per cent of normal kidneys. 4,15,19,21 Such extravasation, which we also have occasionally observed, may be regarded as artificially produced and is excluded from the present series.

6. Finally, those uncommon cases in which an actual rent is produced in the ureter or pelvis by *pressure necrosis of the stone* are excluded.

The term "extravasation" also requires careful consideration and definition. Harrow and Sloane¹⁵ classify the types of renal extravasation into 4 categories: "pyelosinous," "pyelolymphatic," "pyelovenous" and "pyelotubular backflow." However, Fleischner *et al.*¹⁰ do not consider pyelotubular backflow a form of extravasation, but rather a manifestation of increased urinary reabsorption in the papilla.

We have not included cases with pyelotubular visualization in our series. No case of pyelovenous backflow was seen in our material. There remain, therefore, the 2 groups—pyelosinous and pyelolymphatic backflow. Six patients in our series demonstrated both phenomena.

CLINICAL MATERIAL

During the previous approximately 20 years, it has been the practice in this hospi-

tal to perform intravenous pyelography as an emergency procedure in all cases of suspected urinary tract colic. This has proved to be a completely safe procedure and, on many occasions, of considerable diagnostic value. Two hundred and fifty-six such intravenous urographies, made during or immediately after acute colic over the last 10 years, have been reviewed, and 16 cases of spontaneous extravasation of contrast material, fulfilling our above criteria, have been found.

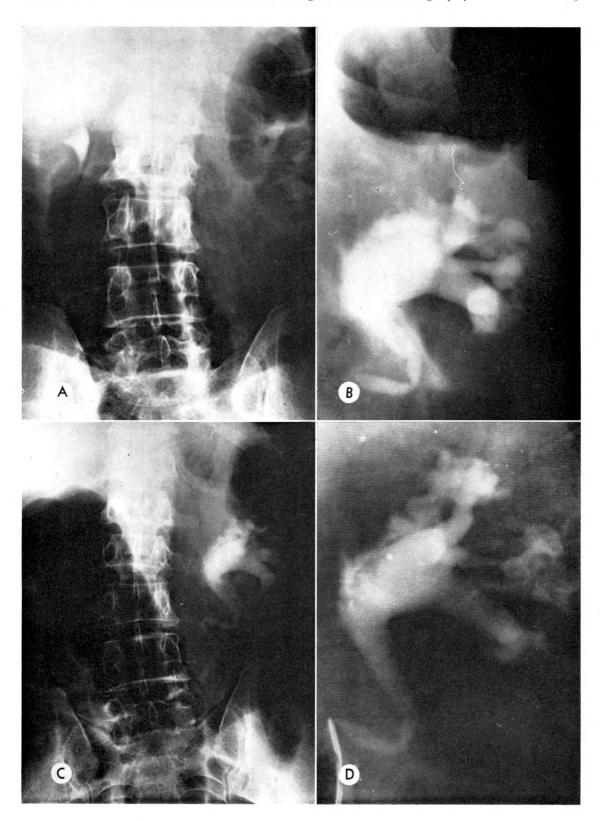
These 16 cases consisted of 12 males and 4 females, and their ages ranged from 21 to 70 years. Extravasation was demonstrated in 8 cases on the right side and in the remaining 8 on the left. The obstructing stone was identified in 8 cases at or very near the ureterovesical junction, in 2 cases in the middle third, and in 4 cases in the upper third of the ureter. In 2 cases, no stone was visible. In 3 patients the largest diameter of the stone was over 3 mm. and in 11 it was smaller.

The intravenous urograms were obtained from 2 hours to 4 days after the beginning of the acute renal colic episode. In some cases, medication to relieve the pain had been given before urography was started, but the urographic examination itself was made during an actual attack of pain or shortly afterwards. In 12 cases repeat intravenous urographies, were performed; in 5 within 3 days of the first intravenous pyelography, in 2 within 10 days, in 2 within 30 days, and in 3 within 1 year. In 1 case retrograde pyelography was performed the day after intravenous urography. This was actually the first case of the series,

Fig. 1. G.M., a 60 year old male, complained of sharp left loin pain, but had no colic. Intravenous urography was performed on June 29, 1958, 4 hours after the beginning of pain. No calculus was visible. (A) Ten minute study shows indistinct upper calyces on the left and contrast material outlining the infundibula. The psoas shadow on the left is absent. (B) Seventy minute close-up pyelogram shows unsharp calyces and a great quantity of contrast material around the pelvis and upper ureter. Streaky lines are visible at the upper calyces corresponding to lymph vessels. The walls of the pelvis and upper ureter are visible as thin radio-lucent lines. (C) Eight hours after injection, pyelogram still shows marked peripelvic and periureteral extravasation. Note the elongated pipe ureter. (D) Left retrograde pyelogram again shows the extravasa-

tion from the upper calyces and contrast material around the pelvis.

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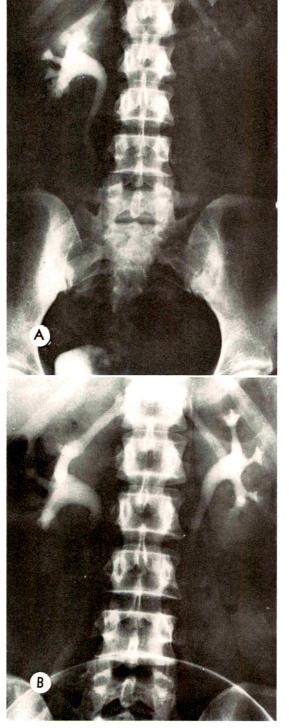


Fig. 2. S.L., a 37 year old female, was examined during a right sided urinary colic attack. (A) December 26, 1964: 120 minute urogram shows marked

when the appearance on the initial intravenous pyelogram was not fully understood. In the remaining 3 cases, no follow-up examination was obtained since the patients failed to return. Additional urograms were available in a number of patients who were referred, at a later date, for evaluation of the urinary tract for other reasons, *e.g.*, prostatic symptoms, postoperative control, or urinary infection. In all, a total of 38 urograms was obtained in the 16 patients from the time of their first attack of colic.

ROENTGEN FINDINGS

In 14 of the 16 patients extravasation was demonstrated during the first intravenous pyelography. In the remaining 2, there was no evidence of extravasation at the time of the first study, but it was demonstrated 36 and 48 hours, respectively, after the onset of the colic episode. In both cases, the stone was still present in the ureter at the time of the second examination.

In 13 cases, extravasation was visualized during a first episode of renal colic and in 3 cases during the second such episode.

The extravasation was first seen on the 10 minute urogram of the series in 7 patients, up to the 1 hour study in 7 cases, and after 1 hour in 2 cases.

The appearance of extravasation varied from case to case. The mildest type, that described by Olsson²¹ as "hornlike," was seen in 3 cases. The remaining 13 cases all had varying degrees of pyelosinous extravasation, in 6 of whom an associated delineation of lymphatic channels was also present.

intrarenal extravasation around the upper calyces and to a lesser degree around the lower calyx. Note the fine streaky linear shadows extending from the upper half of the kidney towards the spine corresponding to lymph vessels. The whole length of the elongated ureter is visible (pipe ureter). The right psoas shadow is blurred. (B) January 15, 1965: Intravenous urogram after 30 minutes of compression shows normal pelvicalyceal system bilaterally. The right psoas shadow is still indistinct.

These lymph vessels ran between the medial border of the kidney and the spine in 2 cases (Fig. 1B and 2A), while in the remaining 4 cases channels corresponding to intrarenal lymph vessels were observed (Fig. 3B). All the cases in which lymph vessels were seen had a marked degree of pyelosinous intrarenal extravasation, and in 3 of them there was a pronounced retroperitoneal extension as well (Fig. 1C). In all, extrarenal retroperitoneal extravasation of the contrast material, which collected around the pelvis and ureter, was seen in 6 cases.

Subcapsular deposit of contrast material was seen in I case only, in conjunction with marked pyelosinous extravasation extending into the retroperitoneal space along the ureter. This deposit remained visible for 8 hours, and was again visualized when the patient was re-examined 36 hours after the colic attack (Fig. 4, A–D).

In I interesting case, which is discussed in greater detail below, extravasation progressed to form a pararenal pseudocyst which displaced the kidney and upper ureter anteriorly, laterally and cranially (Fig. 7, A, B and C).

In all cases extravasation was observed for the duration of the urographic examination, lasting up to 3 hours, and in 3 cases it was still visible on delayed roentgenograms taken 5, 14, and 24 hours, respectively, after the administration of the contrast material. In 3 patients, extravasation was still seen on repeat intravenous uro-

grams 2 days (Fig. 4, A-D; and 7, A, B and C) and 3 days after the initial intravenous pyelography. None of these patients had colicky pains at the time of the second examination, but in all of them the stone in the ureter was still visible. In 2 of the pa-



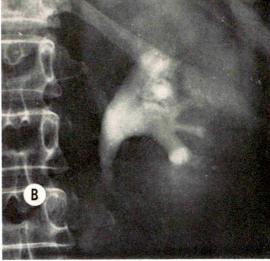


Fig. 3. F.L., a 56 year old female. Intravenous pyelography performed during left sided urinary colic attack. (A) Sixty minute urogram shows a marked left nephrogram, a calculus just above the transverse process of L3, and a moderate dilatation of the pelvicalyceal system. Note the dilated and slightly indistinct upper calyx. (B) One hundred and 20 minute pyelogram, close up view, shows almost complete disappearance of the upper calyx, and multiple streaky lines between the upper and middle calyces due to filling of intrarenal lymphatics.

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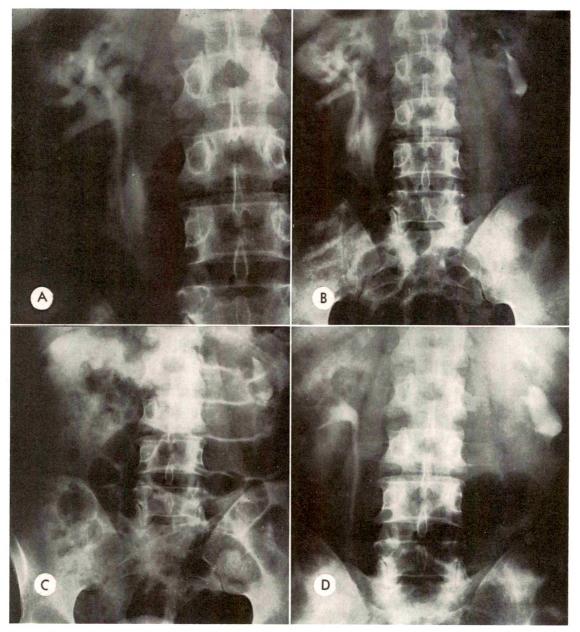


Fig. 4. G.A., a 51 year old male. Intravenous urography was performed on the evening of May 14, 1963, during an acute right urinary colic attack. (A) Thirty minute study shows contrast material around the upper calyces, pelvis and proximal ureter. The calyces are slightly dilated. The psoas shadow is indistinct. (B) Sixty minute study shows contrast material outside the upper calyces reaching the borders of the kidney shadow (subcapsular). The quantity of peripelvic and periureteral contrast material is increased. (C) One hundred and twenty minute study of second intravenous urography on May 16, 1963, 36 hours after the first, shows a large quantity of contrast material subcapsularly outlining the upper pole. The right psoas shadow is blurred. (D) Ten minute study on May 17, 1963 (60 hours after first and 24 hours after second intravenous pyelography) shows normal collecting system on the right and a normal appearing right psoas shadow.

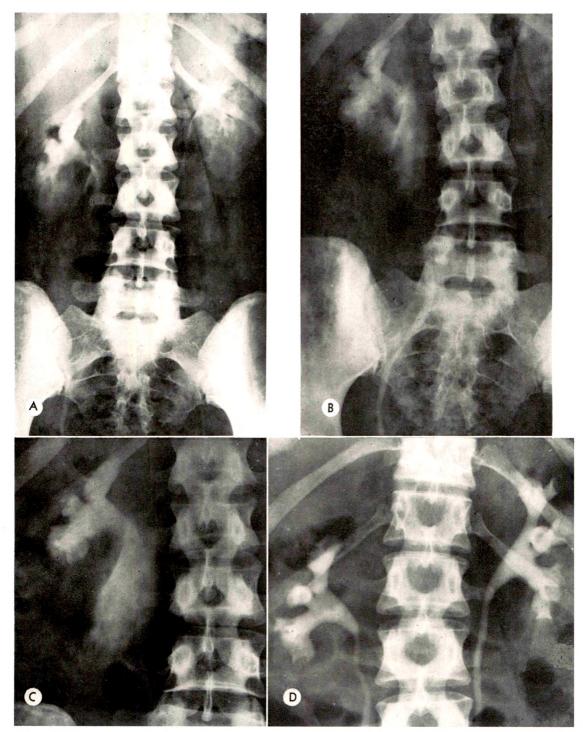


Fig. 5. M.T., a 21 year old female. Intravenous pyelography performed on August 27, 1959, 4 hours after cessation of an acute colic attack; pain still present. (A) Ten minute study shows a somewhat dilated pelvicalyceal system, blurred lower calyces and some extravasation around the pelviureteral junction on the right. The right psoas shadow is blurred. The ureter is visible. (B) Thirty minute urogram shows marked extravasation around the lower calyces and a great quantity of contrast material around the upper ureter. The ureter is visible in its entire length (pipe ureter). (C) Forty-five minute close-up view shows an increase of the periureteral extravasation. Note the fine radiolucent lines between the contrast material within the ureter and the one outside of it. The radiolucent lines represent the wall of the ureter. (D) Forty-five minute intravenous urogram on December 3, 1959 after 30 minutes of compression shows a normal pelvicalyceal system bilaterally. The right psoas shadow is still blurred.

tients, a third intravenous pyelographic study, performed 4 and 9 days, respectively, after the second showed a normal collecting system without spontaneous

extravasation. In 5 patients, external ureteral compression was applied for 30 to 40 minutes during repeat intravenous pyelography, 2, 7, 20, 36 and 96 days,

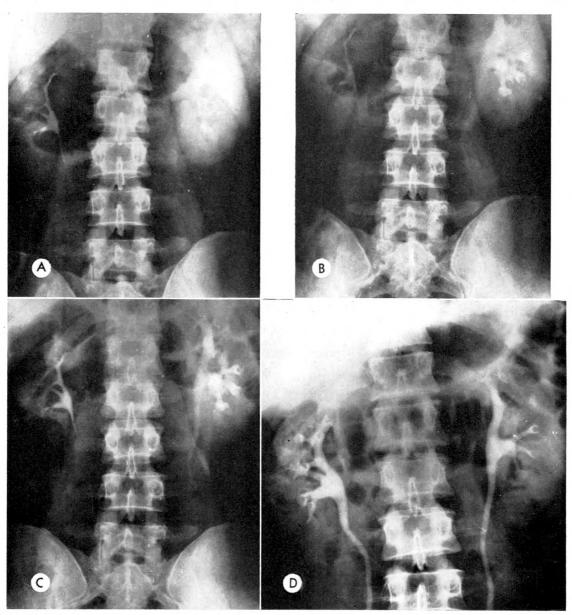


Fig. 6. J.T., a 26 year old male. Intravenous pyelography performed 2 hours after beginning of a left acute urinary colic attack on November 22, 1963. (A) Ten minute study shows a marked nephrogram and practically normal calyces. The psoas shadow is normal bilaterally. (B) Thirty minute study shows blurred lower calyx and streaky irregular lines around infundibula of the lower calyces. There is contrast material around the upper ureter. The wall of ureter is visible as fine radiolucent parallel lines. A nephrogram with less intensity is still present. (C) One hundred and twenty minute study shows less intrarenal extravasation. Note contrast material along the psoas shadow between transverse processes of L3–L4. The nephrogram nearly disappeared. (D) Forty minute study on November 24, 1963 after 30 minutes of compression shows normal collecting system bilaterally.

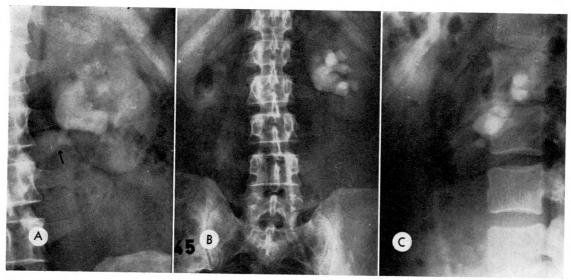


Fig. 7. G.A., a 52 year old male. Intravenous urography was performed on May 14, 1957, two weeks after colic attack. A small stone was present at the ureterovesical junction. (A) Sixty minute study shows moderate hydronephrosis and peripelvic and periureteral (arrow) extravasation on the left. (B) Forty-five minute urogram on May 16, 1957, again shows the peripelvic extravasation. The psoas shadow on the left is absent. There is a soft tissue mass below the left kidney. The left ureter is displaced toward the mid-line. (C) Left lateral exposure shows marked anterior displacement of the ureter.

respectively, after the colic attack. Only in I of these (7 days)—belonging to the group of 3 who showed spontaneous extravasation on the second intravenous pyelographic study—did extravasation of the pyelosinous type appear. No extravasation was seen in the other 4 patients. As mentioned above, in 1 patient a retrograde examination was performed 24 hours after the intravenous urography. This showed the same extravasation as seen on the urogram, although no obstruction whatsoever to the catheter was felt (Fig. 1D). Fluoroscopy during the retrograde injection revealed contrast material flowing out from the upper calvces, although the injection pressure was low (manual injection, pressure not recorded by manometer). Apart from the finding of extravasation in these patients, increased opacification of the affected kidney (nephrographic effect) was seen in 10, being marked in 5 and mild in the remaining 5 (Fig. 3, A and B; and 6, A–D). Despite the nephrographic effect, delineation of the pelvicalyceal system was observed in all cases. The collecting system was slightly dilated in 13 cases and moderately dilated in the other 3 patients. In no case was there a marked hydronephrosis or hydroureter. In all patients who had repeat examinations, the urinary tract ultimately returned to normal. In this group were 2 patients upon whom operations were performed, one for removal of a renal pseudocyst and the other a uretero-lithotomy.

In I case a definite collapse of the calyces and pelvis was observed (Fig. 8, A and B). This was demonstrated on a roentgenogram showing pyelosinous extravasation with extension upon the psoas. The 10 and 30 minute studies showed dilated calyces and no extravasation but on the 75 minute urogram and on the following ones up to 180 minutes, the calyces were small and extravasation was present. This 28 year old patient had suffered from nephrolithiasis and ureterolithiasis for a period of 5 years prior to his present colic attack. Unfortunately, he has not returned for follow-up examination.

The psoas shadow on the affected side was normally sharp in only 2 of the cases showing extravasation (Fig. 6, A, B and C). In the other 14 patients it was indistinct in

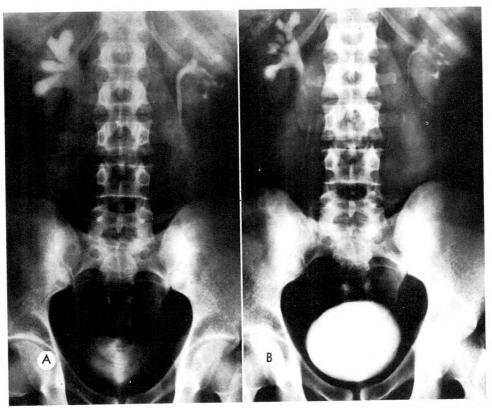


Fig. 8. T.N., a 28 year old male, was examined shortly after an acute right urinary colic attack. He still had marked flank pain during the examination. A 10 by 6 mm. stone was demonstrated at the level of the first sacral segment. (A) Thirty minute urogram shows smoothly outlined dilated calyces and pelvis on the right. No extravasation is visible. (B) At 145 minutes after injection, a marked diminution of all calyces and pelvis, extravasation around lower calyx, small deposit of contrast material around upper ureter and dense bulge on the psoas shadow opposite L2 are visualized.

part or all its length (Fig. 1 through 5; and 7 through 8).

DISCUSSION

Spontaneous extravasation of contrast material during intravenous urography has rarely been described, and previous reports dealing with this phenomenon have been based on only few cases. Close scrutiny of these cases reveals that a number of them does not fulfill the strict criteria we have described. Some have been subjected to retrograde examination less than 3 weeks prior to intravenous examination, 20,33 to previous surgery, 11,16 or compression. 32

There is a certain amount of confusion in some reports between extravasation and rupture of the renal pelvis or ureter. The cases described by Persky and Joelson,²⁴

Schick and Shea³³ and Weiner et al.,³⁴ for example, are reported as spontaneous rupture of the renal pelvis due to calculus obstruction, but the urogram actually shows forniceal rupture with peripelvic and periureteric pyelosinous extravasation. On the other hand, there are cases in which an actual rent of the pelvis27,28 or ureter23 occurred, and yet they are reported as cases of spontaneous extravasation. A clear distinction between forniceal rupture with extravasation, on the one hand, and an actual rent of the renal pelvis or ureter, on the other hand, appears to be important from the therapeutic point of view. Whereas in the former case, the vast majority of patients require no specific treatment for the extravasation, which resolves and absorbs spontaneously, in the latter case there is a =

much greater likelihood that surgical intervention will be necessary.

The differentiation between these two entities may be aided by certain observations. The first is to look specifically for contrast material around a calyx, the presence of which clearly points to forniceal rupture. Secondly, the demonstration of the ureter seems to us to be a helpful point in the differential diagnosis. In cases showing actual rents reported in the literature, 6,23,27,28 the ureter on the affected side was never visualized, whereas in all our cases showing pyelosinous extravasation a typical "pipe" ureter was present (Fig. 1 and 2; and 4 through 7) and remained delineated for as long as 24 hours after injection in some of the cases. Re-examination 24 to 48 hours after the onset of an attack will show, in most cases of forniceal rupture, disappearance of the extravasation, while in cases of actual rent or perforation of the pelvis or ureter, the roentgenologic appearance remains unchanged. This, however, is not without exception, as exemplified by 3 of our patients in whom, as recorded above, extravasation persisted 2 and 3 days after the colic attack. Clinically, also, there is a difference. Patients with an actual rent of the pelvis or ureter tend to appear more ill and have a higher temperature and white blood cell count than do those with extravasation.28

In addition to the 3 patients showing recurrent or persistent extravasation on intravenous pyelograms, we have referred to another case in which, on retrograde examination 24 hours after the colic episode, an exact reproduction of the extravasation as seen on the intravenous urogram was obtained (Fig. 1D). We have also stated that in another patient the extravasation was reproduced, 7 days after the onset of the colic and 4 days after its termination, by external ureteral compression for 40 minutes. All these patients showed on the final examination a normal collecting system and appeared clinically well on prolonged followup. Thus, our experience is at variance with Politano's statement that reproduc-

tion of the changes on repeat examination bespeaks some disease process in the kidney, since, in his opinion, it is most unusual for the pyelorenal backflow phenomenon to be demonstrated on a second series of intravenous urograms. In our material of 16 cases, the extravasation was demonstrated in 4 cases (25 per cent) within 72 hours of the onset of the colic. It could be reproduced by compression in I additional case within 7 days. It was not reproducible, even with prolonged compression, in 4 cases, 2, 20, 36 and 96 days, respectively, after the onset of the colic. It seems to us, therefore, that the demonstration of the extravasation in repeat intravenous urograms or retrograde pyelograms is not unusual and cannot serve as a reliable differential sign between spontaneous pyelosinous backflow in a healthy kidney and organic disease of the calvx.

It is possible that urinary extravasation into the perirenal and periureteral retroperitoneal space might set up an inflammatory reaction, or even cause the formation of an abscess. We have not seen the development of such an abscess in any of our patients, but in I case, referred to briefly above, we did observe the development of a pararenal pseudocyst 3 weeks after an acute urinary colic attack (Fig. 7, A, B and C). The pseudocyst, which was $20 \times 15 \times 12$ cm. in size, was clinically palpable. It was excised at operation, contained clear urine, and pathologic examination of the extirpated walls showed chronic nonspecific inflammation. No rent or tear of the pelvis or ureter was found. Apart from excision of the cyst and drainage of the area, no other manipulation was necessary. Recovery was rapid and uneventful, the calculus passed spontaneously, and intravenous pyelography, 2 months later, was entirely normal.

It is noteworthy that the clinical course of this patient appeared much more serious than that seen in the other 15 patients, with increasingly severe attacks of pain, fever, rigors, and a raised leukocyte count and erythrocyte sedimentation rate. We believe that this is the first case in which a

pararenal pseudocyst was observed which developed after acute renal colic, with pyelosinous extravasation but without an actual rent or perforation of the pelvis or ureter.^{2,81} This case emphasizes the importance of repeat urographic examination after urinary colic.

There is some discussion as to the mechanism of the extravasation due to colic or prolonged ureteral compression. It is generally agreed that the basic etiologic factor is a suddenly raised intrapelvic pressure. Forsythe and his co-workers¹¹ believe that contrast material first enters the lymphatics, from which it escapes when their capacity has been exceeded. However, our experience shows quite clearly that the contrast material collects at the beginning of the examination around the calvx and in the sinus renalis, and only later, if at all, are the lymph vessels visible. This observation was made in 6 of our cases. Moreover, in the case in which retrograde pyelography was performed, we observed on the screen and spot roentgenograms during the retrograde injection the appearance of contrast material first around the calyces and pelvis, and only later in the lymphatics. It is, therefore, likely that contrast material collects first in the renal sinus and then enters the lymphatics, and not vice versa.

Forniceal rupture may occur very early during a renal colic episode. This is illustrated by I of our patients in whom, in an intravenous urogram made only 2 hours after the onset of pain, marked extravasation was already apparent on the 30 minute study (Fig. 6, A-D). Our cases with persistent extravasation on repeated examination show that it may take a considerable time for the forniceal rupture to seal off, and it is likely that retroperitoneal extravasation of urine may continue for many hours, or even days. This extravasate is being continuously reabsorbed and reexcreted by the kidneys. This accounts for the unusually prolonged visualization of the collecting system of the unaffected kidney as well in such cases. It seems probable that the appearance of the psoas

shadow is a good indicator of the presence of extravasation. In 12 of our cases, the psoas shadow on the affected side was blurred on the initial examination, in 2 cases it was normal, and in 2 cases it was normal at the first examination and appeared blurred at the second. This blurring cleared and the psoas shadow returned to normal in 3 cases, but remained blurred in the remaining II cases for a very long time—even up to I year. A review of all the intravenous urograms made during acute urinary colic attacks showed some blurring of the psoas shadow in approximately 50 per cent of them, from which it appears likely that some degree of extravasation does occur relatively frequently. Such a conclusion would be well in accord with Dallenbach's⁷ observation concerning the development of "urinary precipitates" in instances of acutely raised pressure in the upper renal tract. The fact that the actual visualization of this extravasation is uncommon is probably due to the quantity being small, or because intravenous urography is performed some time after the cessation of the colic episode when the fornix rupture has already sealed off. Such a conclusion is also supported by the appearance of the "wet" retroperitoneal space often found on exploration after an attack of acute renal colic. 14,16

The relative absence of any marked hydronephrosis during and after acute renal colic attacks, even when prolonged, seems to support this theory as well—the fornix rupture being an escape route for the pelvic contents and relieving the intrapelvic pressure. One case, in which we could actually visualize "collapse" of the dilated pelvicalyceal system on urograms during acute renal colic, with subsequent appearance of the contrast material on the psoas, has already been referred to above (Fig. 8, A and B), clearly indicating that the fornix rupture prevented further dilatation of the pelvicalyceal system.

SUMMARY AND CONCLUSIONS

Attention is drawn to the entity of spon-

taneous pyelosinous extravasation from the kidney during an attack of acute urinary colic, and the condition is illustrated by 16 personal cases.

Strict criteria for use of the term "spontaneous" are listed, and the term "extravasation" is defined.

Extravasation may be demonstrated early or late in the attack, and may sometimes persist for days.

A distinction is drawn between spontaneous renal extravasation and leakage due to a rent from the pelvis or ureter.

In our material, the persistence of extravasation on repeat examination did not necessarily indicate a diseased kidney.

A case in which the extravasation proceeded to the formation of a pseudocyst is recorded. This appears to be the first such case described without a pelvic or ureteral rent.

Evidence is adduced that lymphatic filling is secondary to the extravasation.

It is probable that a degree of spontaneous extravasation is a relatively common occurrence during acute urinary colic, and may explain the relatively mild degree of dilatation above the acute obstruction and the frequent finding of "wet" retroperitoneal tissue in such cases on operation.

The value and safety of intravenous urography during an attack of urinary tract colic are emphasized. If this examination is routinely performed, as in our opinion is desirable, an increasing number of cases of spontaneous renal extravasation will be detected. The appearance and nature of this phenomenon should be recognized and distinguished from pelvic or ureteral rupture. The occurrence of extravasation is not in itself an indication for any specific therapy, but requires adequate follow-up to ensure its disappearance, to exclude underlying renal disease, and to exclude the late development of a complication, such as pseudocyst.

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PERIPELVIC EXTRAVASATION DURING INTRAVENOUS UROGRAPHY*

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PERIPELVIC extravasation refers to the roentgenographic demonstration of contrast medium outside the pelvicalyceal system but within the renal sinus adjacent to the pelvis. Occasionally, the extravasation may extend downward along the ureter or the psoas muscle.

It is a rare finding on excretory pyelograms. In 1948, Olsson⁹ reported the first series of cases, 6 examples of this condition, all occurring in patients with renal colic, in a series of 100 cases of backflow seen on excretory urograms. The total number of cases reported to date is approximately 37, depending on the interpretation of certain cases.^{2–10,14,15}

Peripelvic extravasation occurs as a result of ureteral obstruction, usually secondary to a calculus. It is important to recognize it since conservative therapy is indicated in almost all instances.

In the past 2 years, we have seen 4 cases of peripelvic extravasation during intravenous urography at The Christ Hospital, all occurring in patients suffering from renal colic. All of the examinations were performed without abdominal compression.

REPORT OF CASES

Case I. F. U., a 66 year old woman, was admitted to The Christ Hospital on July 13, 1963 with a 4 hour history of left renal colic with nausea and vomiting. Her temperature was 98.0° F. Physical examination revealed only left costovertebral angle tenderness. Urinalysis showed many white blood cells but no red blood cells. Leukocyte count was 15,300 with a slight left shift. An intravenous pyelogram the day after admission showed slight hydronephrosis on the left with fullness of the left ureter down to about I cm. above the bladder. There was extravasation of the contrast medium about the renal pelvis (Fig. 1). A retrograde pyelogram

on the next day, using about 7 cc. of contrast medium, showed a similar pattern of extravasation (Fig. 2). The patient had no discomfort during the procedure. The walls of the upper pole infundibulum were well outlined. Two days later an excretory urogram showed no extravasation or other abnormality (Fig. 3). Urine culture obtained at the time of the retrograde pyelogram revealed no growth. The patient was treated with antibiotics and made an uneventful recovery. No stone was recovered.

Case II. J. N., a 44 year old man, was admitted to The Christ Hospital on July 23, 1963 with a 6 hour history of left renal colic and increasing dysuria. For the previous 4 months he had had intermittent left upper abdominal pain, marked hesitancy, dysuria, frequency and nocturia, all of which had been getting worse. Twelve years earlier he had had a bout of right renal colic. An intravenous pyelogram at that time showed no evidence of stone and none was recovered.

On the present admission the patient was afebrile. There was tenderness at the left costovertebral angle and in the left upper abdomen. Urinalysis showed 2–3 white blood cells and 2–3 red blood cells per high power field. White



Fig. 1. Case 1. Intravenous pyelogram (15 minute film). There is moderate hydronephrosis with peripelvic extravasation on the left.

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Fig. 2. Case 1. Left retrograde pyelogram. Peripelvic extravasation is similar to that in Figure 1. The walls of the upper pole infundibulum are well outlined.

blood count was 14,300 with 70 per cent neutrophils and 6 per cent band forms.

An intravenous pyelogram on the day of admission showed slight hydronephrosis on the left with extravasation about the pelvis and



Fig. 3. Case i. Intravenous pyelogram (5 minute film). Normal.

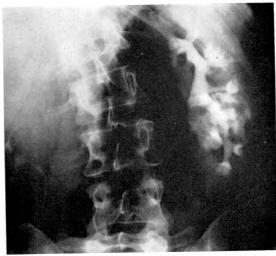


Fig. 4. Case II. Intravenous pyelogram (15 minute film). There is hydronephrosis and extravasation of the contrast medium on the left. Findings of medullary sponge kidneys are more obvious on the same side.

several calyces and evidence of bilateral medullary sponge kidneys (Fig. 4). On the following day a retrograde study showed no extravasation (Fig. 5). The patient's pain was reproduced by distention of the renal pelvis. Three days later a repeat intravenous pyelogram showed bilateral medullary sponge kidneys but no extravasation. The patient was treated with antibiotics and recovered without further incident. A urine culture was negative and no stone was recovered. An intravenous pyelogram performed 18 months later again showed the medullary sponge kidneys without other abnormality.

CASE III. J. H., a 72 year old man, was admitted to The Christ Hospital on January 4, 1965 with the sudden onset, 20 hours before, of urgency and frequency followed by left renal colic, nausea and vomiting. His temperature was normal and physical examination showed only left lower abdominal tenderness. Urinalysis revealed up to 15 red blood cells and a similar number of white blood cells per high power field. Blood count showed 11,200 white blood cells with a slight left shift. An intravenous pyelogram on the day of admission showed delayed function with slight dilatation of the pelvis and calyces on the left. On the 45 minute roentgenogram (Fig. 6), there was extravasation about the pelvis, which was still present 3 hours later. On the following day a stone was extracted from



Fig. 5. Case II. Retrograde pyelogram. No extravasation demonstrated.



Fig. 7. Case III. Retrograde pyelogram. The peripelvic extravasation is similar to that in Figure 6, although the medial wall of the renal pelvis is better outlined.



Fig. 6. Case III. Intravenous pyelogram (45 minute film). The extravasated contrast medium obscures the renal pelvis borders. Right side normal.



Fig. 8. Case IV. Intravenous pyelogram (45 minute film). Contrast medium is seen adjacent to the pelvis as well as extending downward along the psoas muscle. Right side normal.



FIG. 9. Case IV. Intravenous pyelogram (10 minute film). There is moderate hydronephrosis on the left but no extravasation. Right side normal.

the left ureter. The subsequent retrograde pyelogram showed a similar pattern of extravasation (Fig. 7). A catheter was left in the renal pelvis and the patient received antibiotics and supportive therapy. He recovered without complication. Urine culture was negative. No further studies were obtained.

Case IV. R. K., a 60 year old man, was admitted to The Christ Hospital on February I, 1965 with a 7 hour history of somewhat colicky pain in the area of the left costovertebral angle. On physical examination, there was tenderness over the left costovertebral angle and spasm of the abdominal muscles. Temperature was normal. Urinalysis showed 5–6 white blood cells and an occasional red blood cell per high power field. Leukocyte count was 8,300 with 83 per cent neutrophils. An immediate intravenous pyelogram showed hydronephrosis on the left. Extravasation was first noted on the 5 minute study; on the 45 minute roentgenogram (Fig. 8). the extravasation extended downward along

the psoas muscle. A repeat study the following day showed no extravasation but the left pelvicalyceal system was still distended (Fig. 9). Two days later a small stone was found in the bladder at cystoscopy. A retrograde pyelogram at that time was normal. Urine culture was negative. The patient did well on antibiotics and supportive therapy.

DISCUSSION

The finding common to all of the reported cases of peripelvic extravasation is ureteral obstruction. This may be manifest by delayed function and/or dilatation of the pelvis on the involved side. Renal colic is almost always present and in approximately one-half of the cases a ureteral stone has been found. In the remainder, although many of the signs and symptoms indicate a stone, none has been recovered. In a few cases, ureteral obstruction has been due to other causes, *i.e.*, complications of pelvic surgery.

The mechanism of peripelvic extravasation is not definitely known. There is general agreement that the contrast medium passes from the fornix of one or more calyces into the renal sinus and, in some cases, into the retroperitoneal space via the renal hilus. Exactly how this occurs is still not clear. Three possibilities have been proposed:

I. Olsson,¹⁰ having seen 14 cases, concluded that the extravasation was secondary to rupture of a fornix and as such was "an integral part of the pathophysiological unit constituting the renal colic." In support of this theory, he quotes the pathologist, Hamperl, who found tears in the region of the fornix in kidney specimens from patients suffering from renal colic. Harrow

2. Hinman,⁶ after reviewing 23 cases from the literature and 5 of his own, felt that this condition was "an extreme form of pyelosinous backflow" as opposed to rupture of the renal pelvis. Three of his cases had intravenous pyelograms showing extravasation which was not demonstrated on the subsequent retrograde studies per-

and Sloane⁵ agree with this explanation.

formed within 24 hours. Three of his cases were operated upon and no abnormality of the renal pelvis was found in any of them.

3. Others have invoked the renal lymphatic drainage to explain this condition. They base their theory on the concept that the renal lymphatics act as a safety valve mechanism in ureteral obstruction, carrying off excess fluid from the kidney. Fine and Vermooten⁸ postulated rupture of over burdened lymphatics as the cause of the extravasate.

Most authors use the term "backflow" to indicate passage of contrast medium from the pelvicalyceal system into the adjacent tissue without stating how this occurs. It is thus applicable to a wide variety of conditions. Politano¹¹ points out a very important qualification, noting that backflow is rarely reproducible, whereas changes that are readily reproducible on subsequent urographic examinations are usually due to some disease process or structural defect. Narath⁸ uses somewhat different terms to express the same concept. He suggests that, when contrast medium is noted outside of the pelvicalyceal system, an immediate retrograde study be performed to differentiate rupture from backflow. If there is a rupture present, the findings should be reproduced; if the finding merely represents backflow, extravasation will not again be seen. Hinman implies this same conclusion. In the few reported cases of peripelvic extravasation with immediate follow-up retrograde studies, \$,4,6 extravasation has not been demonstrated.

All 4 of our cases had follow-up studies approximately 24 hours after the initial intravenous pyelograms. In 2 of these, retrograde studies showed a similar pattern of extravasation (Fig. 2 and 7); while in the other 2, one a repeat intravenous pyelogram, no extravasation was demonstrated (Fig. 5 and 9).

In the differential diagnosis, the most important condition to consider is spontaneous rupture of the renal pelvis itself, since this usually calls for prompt surgical intervention.^{1,12,13} Spontaneous rupture of

the renal pelvis almost always occurs in a kidney which is affected by some underlying pathologic process, such as chronic infection. The patients are usually acutely and seriously ill. A flank mass may be palpable and this may enlarge over a period of time. The underlying process affecting the kidney is frequently manifest on excretory or retrograde pyelography and when seen should bring the possibility of rupture to mind. In the otherwise normal kidney, the extravasation is much more likely to originate at a fornix, and the site is sometimes seen on the roentgenograms. In our cases, as well as in most of the reported ones, the patients were not severely ill except for renal colic; they were afebrile and none was in shock.

Conservative therapy, with relief of the obstruction where possible, *i.e.*, removal of the stone, is all that is necessary in most instances. On several occasions, operations have been performed for a suspected rupture and none has been found. 4.6.14 Evidence thus far indicates that surgery should be considered only when the obstruction cannot be relieved by other means, as in the cases of postoperative obstruction. Forsythe *et al.*4 reported 2 cases of lower ureteral obstruction complicating pelvic operations. In both cases excretory urography showed peripelvic extravasation. After corrective surgery, the urograms returned to normal.

In the assessment of a given case, retrograde pyelography should be considered as a means of differentiating backflow from rupture of a fornix.

SUMMARY

Backflow, in the usual context, is a general term referring to the passage of contrast medium from the pelvicalyceal system into the kidney. In a more restricted sense, it refers to such passage without actual rupture of the pelvicalyceal system itself.

Peripelvic extravasation refers to the presence of contrast medium outside of the pelvicalyceal system, in the renal sinus adjacent to the pelvis. Occasionally, the ex-

travasation may extend downward in the retroperitoneal space along the ureter or psoas muscle. There are two main possibilities to account for this condition: backflow (via a fornix) and rupture of a fornix. In either case the underlying cause is ureteral obstruction, usually secondary to a calculus, with resultant increased pressure in the renal pelvis. Clinically, this is manifest by renal colic.

The most important condition to be differentiated is spontaneous rupture of the renal pelvis itself, as this calls for operation, whereas the condition reported here almost always responds to conservative therapy.

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The author expresses his appreciation to Drs. Benjamin Felson, Professor of Radiology, University of Cincinnati College of Medicine, and Chapin Hawley, Director, Radiology Department, The Christ Hospital, for their helpful suggestions and to Drs. Arthur T. Evans, Albert J. Farrell and Homer H. Kohler for permission to include their patients in this paper.

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SPONTANEOUS URINARY EXTRAVASATION ASSOCIATED WITH RENAL COLIC CAUSING A PERINEPHRIC ABSCESS*

By BENEDICT R. HARROW, M.D. MIAMI, FLORIDA

 $m I^{N}$ 2 recent articles, it is stated that spontaneous peripelvic extravasation of urine is a rare event.1,8 The author, however, has encountered 30 cases in the last 6 years, caused mainly by ureteral stones, 6 cases having been published previously.2,3 It is true that a limited number, only about 46 spontaneous episodes, have been described in past medical writings. Nevertheless, many cases have been presented at local Miami meetings by radiologists and urologists. The occurrence rate has been high and not felt worthy of individual reports. Before the last decade, such incidences of urinary extravasation outside the renal pelvis were not diagnosed because of lack of knowledge of the roentgenographic characteristics, lesser number of excretory urographies performed in renal colic, decreased density of urographic media, less tendency to take delayed roentgenograms and inadequate amounts of injected contrast agents. There can be no doubt about the common occurrence of perirenal extravasation even if not demonstrated on roentgenograms, and the reasons have been presented before.2

Since the extravasation is so frequent, it is more important to understand the causes and effects. Certainly, operative drainage is usually not advisable, although some unnecessary surgical procedures have been performed.² In none of the first 30 cases seen was drainage required and the only treatment was directed to the stone or the other causes of the acute ureteral obstruction. In the thirty-first case, which is reported below, subsequent complications did eventually require operative drainage.

This event also proved for the first time that the pyelosinous, peripelvic extravasation is a cause for perinephric abscesses.

REPORT OF A CASE

D. E., a 20 year old man, was admitted to Mercy Hospital (admission #186957) on March 27, 1965 with a fracture dislocation of a cervical vertebra caused by a dive into shallow waters. Following an emergency cervical laminectomy and cervical fusion, he was immobilized by casts and kept in bed for 2 months. An indwelling Foley catheter was required for 2 weeks and after removal of the catheter he developed fever and pyuria. Under antimicrobial therapy, the fever abated in 5 days, although the pyuria and bacteriuria persisted. The patient made a remarkable recovery with a minimal amount of neurologic residual damage, and after 2 months in bed he was able to walk actively with good muscle strength. After 3 days of ambulation, he suddenly developed severe left renal colic and spiked fevers to 104-105° F. each day.

An excretory urogram on June 8, 1965, after 2 days of fever, showed 2 stones blocking the left ureter at the ureterovesical junction. In addition, there were 2 stones in the upper segment of the left ureter and 2 stones in the middle calyx of the left kidney, each of the stones measuring from 3 to 5 mm. in diameter. Pyelosinous extravasation was readily identified on later roentgenograms, extending around the left pelvis and upper ureter (Fig. 1, A and B). Because the calculi were soft recumbency stones, they were expected to pass spontaneously. Indeed, after 6 days of fever the patient passed and recovered the 2 lower and the 2 upper ureteral stones. Analyses revealed a calcium ammonium phosphate composition. Despite the fact that the 2 calyceal stones remained fixed in place on repeated plain roentgenograms, the patient continued to run a high fever. A repeat excre-

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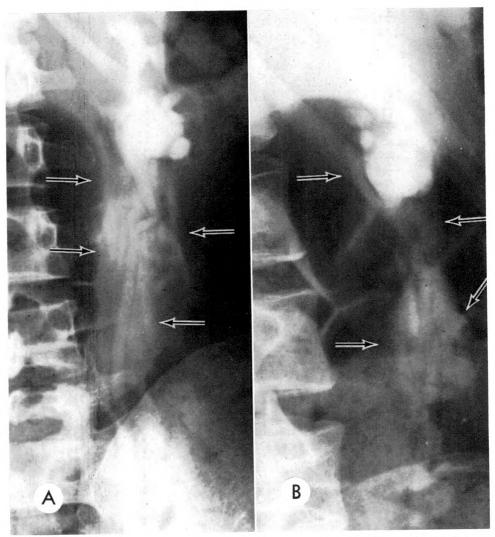


Fig. 1. (A) A delayed 2 hour roentgenogram during excretory urography shows planes of extravasated, contrast-laden urine surrounding the renal pelvis and upper ureter (arrows). The dilated ureter, due to obstructing stones at the ureterovesical junction, is clearly seen and outlined by radiolucent periureteral fat. (B) A left oblique view at the 2 hour period shows the complete encompassing of the pelvis and upper ureter (arrows).

tory urogram on June 12, 1965, taken immediately after passage of the ureteral calculi, continued to show extravasation (Fig. 2).

Still, it was expected that the patient would recover without drainage of the extravasation. He did not, and high fever associated with severe left flank pain persisted. Finally, after 9 days of fever, left retrograde pyelography was performed. This examination demonstrated no residual blockage of the left ureter, but now a mass had developed at the lower pole of the left kidney extending downward and displacing the left ureter medially (Fig. 3). Delayed roentgeno-

grams showed that pyelosinous backflow continued around the pelvis and lower pole of the left kidney. It was apparent that the extravasation had developed into a perirenal abscess. That same day, emergency drainage of a large abscess at the lower pole was performed. At the same time a nephrostomy was carried out and, fortunately, both stones in the middle calyx were found and removed.

The postoperative course was quite satisfactory. Roentgenograms demonstrated no residual stones, and injection of contrast material through the nephrostomy tube on July 2, 1965,



Fig. 2. Despite spontaneous passage of 4 ureteral stones and no further ureteral obstruction, peripelvic and periureteral extravasation (arrows) persisted on a second excretory urogram made 4 days after the first.

the tenth postoperative day, showed the ureter to be patent throughout its entire length. In addition, the abscess cavity had shrunk considerably, although it was still of fairly large size (Fig. 4). Communicating tracts still existed between the abscess and several calyces. Urine cultures continued to grow *E. coli*, the original infecting organism.

After 7 more days, a nephrostogram demonstrated further shrinkage of the abscess cavity (Fig. 5). The patient returned to his home near Albany, New York, and Dr. William Garlick removed the nephrostomy tube. The patient had no further urinary tract problems except that pyuria continued for the next few months. An excretory urogram in September, 1965 showed normal renal and ureteral structures, and by the next month a urinalysis was normal without pyuria or bacteriuria.

DISCUSSION

The mechanism of the pyelosinous backflow extending into the peripelvic regions

has been discussed at length in prior publications^{2,7} and need not be repeated in detail. In essence, any acute ureteral obstruction may lead to high enough pressures to rupture a fornix of a calyx. The urine then escapes through the minute tear in the calyx into the sinus of the kidney alongside the infundibulum of the calvx. The extravasation then readily penetrates a porous leaf of the capsule to escape around the kidney and pelvis of the kidney as depicted in Figure 6. An unusually clear roentgenogram of the actual tract is seen in Figure 7, A and B unequivocally demonstrating the connection between the ruptured fornix of the calyx and the perirenal extravasation. In this instance the pyelo-



Fig. 3. A retrograde ureteropyelogram, 7 days after the first intravenous urogram and 9 days after the initial fever, demonstrates a striking medial deviation of the ureter due to a huge mass at the lower pole of the kidney (arrows).

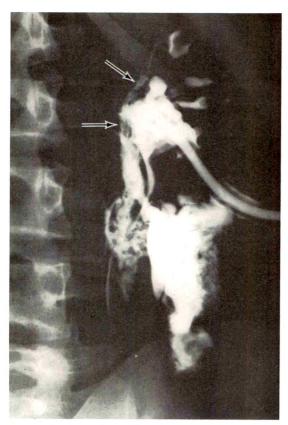


Fig. 4. Injection through the nephrostomy tube 10 days after drainage of the abscess still shows a large cavity with tracts communicating with the upper calyx (arrows).

sinous backflow also originated spontaneously from ureteral obstruction caused by a stone. Once the extravasation occurs, it is absorbed mainly by lymphatics and rapidly disseminated throughout the body as has been shown roentgenographically during retrograde and occasionally intravenous pyelographies. No evidence can be found for a postulated primary rupture of lymphatics as the mechanism of the extravasation. Absorption of the escaped urine in the sinus by veins has been clearly demonstrated during retrograde pyelography utilizing unphysiologic pressures. Spontaneous pyelovenous backflow has never been shown to occur and cannot explain pathologic processes.²

I had postulated that pyelosinous extravasation rather than direct rupture of a cortical renal abscess was a common cause of perinephric abscesses.² Not until this present case could such a mechanism be proved, because in other instances of perirenal abscesses excretory urograms had not been taken in the initial phases. Also, perirenal abscesses have become rare due to antimicrobial therapy and more prompt, efficient methods of handling ureteral obstructions. The case under presentation demonstrates clearly the origin of the pyelosinous backflow from ureteral obstruction and the subsequent development of the abscess despite spontaneous relief of the ureteral obstruction after passage of the

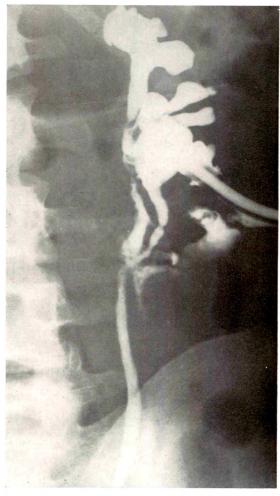
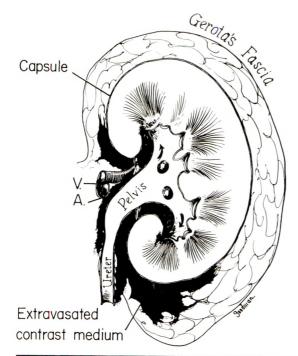


Fig. 5. Finally, 17 days after operative drainage, a nephrostogram demonstrates a considerable shrinkage of the abscess cavity. Note the return of ureter to normal position.



stones. If the patient had not had a preceding chronic urinary tract infection, the extravasation would probably have been reabsorbed without the formation of an abscess. A Foley catheter was properly used for bladder drainage after the accident and was an unavoidable culprit in this instance. Stones formed from recumbency then started the train of events.

Pyelosinous backflow accounts for other types of reaction. A diffuse fibrosis around the renal pelvis and upper ureter can form

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Fig. 6. The rupture through the fornices of calyces and the spread of urine into the renal sinus are depicted in this schematic diagram. The urine penetrates a porous leaf of the pelvis and flows into the perirenal fat between the renal capsule and Gerota's fascia. V. = vein; A. = artery.

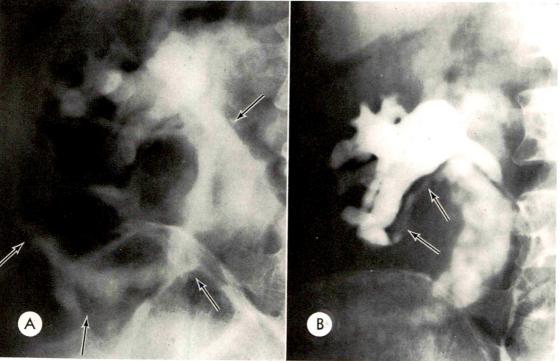


Fig. 7. (A) Arrows point to contrast-laden urine dissecting through the hilus of the right kidney into peripelvic and perirenal fat on this 1 hour roentgenogram during an excretory urography. The pyelosinous backflow was caused by lower ureteral obstruction from a stone. (B) A later retrograde pyelogram demonstrates that the extravasation continues and the actual tract (arrows) communicating with the fornix of the lower calyx is seen more clearly than on the original excretory urogram. The patient subsequently passed a small stone spontaneously and follow-up urograms were normal. (Reproduced by permission from the Southern Medical Journal.)

and can be mistaken for idiopathic retroperitoneal fibrosis. The localized and unilateral distribution not involving the great vessels should provide the differentiation. Renal liposclerosis occupying the sinus and strictures of the upper ureter as well as the infundibula of the calyces have been identified as after effects of extravasation.²

Physicians have been puzzled by the fever and leukocytosis that accompany many episodes of renal colic, although no urinary tract infection can be demonstrated. Dehydration has not taken place in many instances and cannot explain the fever and elevated white blood cell count. Because the fever and leukocytosis have been temporarily related to episodes of severe colic, I believe that pyelosinous backflow and the resultant reaction account for the fever when no infection has been present. In a few circumstances, the low grade fever occurring during right-sided colic may contribute to the physician's impression of a diagnosis of appendicitis, since the urinalysis may be normal. Here, an immediate, emergency excretory urogram solves the problem.4 The pain of renal colic is due to obstruction, not ureteral spasm,

so that evidence of obstruction is invariably present when the urogram is taken during the episode of pain.⁵

Extravasation has been encountered not only with acute ureteral obstruction from varied processes, but also in the presence of other renal diseases. Figure 8, A and B shows an excretory urogram in which pyelosinous extravasation has been produced by a stone blocking the pelviureteral junction. The escaping urine spread around the lower pole of the kidney, outlining a large mass. At operation, the mass was found to be a large cyst with other smaller cysts scattered in the upper and middle poles of the kidney.

Pyelosinous backflow can definitely be produced by severe abdominal compression as used in excretory urography. However, in 3 cases it required at least 20 minutes and usually longer of the severest pressure before backflow resulted. Most patients will not tolerate this amount of abdominal compression. Moreover, as ordinarily used, the compression is applied for only 4 to 8 minutes. Some authors have objected to the use of compression because of artefacts such as pyelosinous backflow.

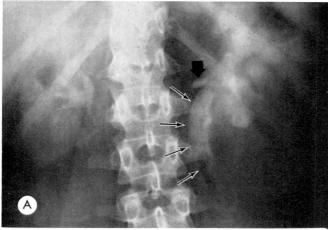
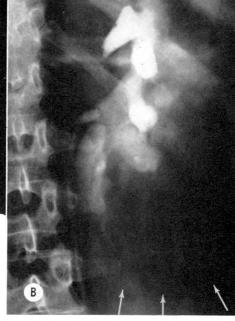


Fig. 8 (A) Intravenous urogram demonstrates a stone blocking the pelvoureteral junction on the left (black arrow). Arrows point to extravasation around a large mass at the lower pole of the kidney. (B) Retrograde ureterogram shows the relationship of the extravasated urine to the ureter, pelvis and mass (arrows), which at operation proved to be a large cyst.



With reasonable care, backflow does not occur and artefacts are easily ferreted out on subsequent roentgenograms taken after the removal of compression. Compression urography has such great advantages and obviates so many retrograde pyelographies that it should not be discarded for such minor objections.⁶

SUMMARY

Pyelosinous extravasation commonly results from acute ureteral obstruction. Ordinarily, operative drainage is not called for, but in I case a perinephric abscess resulted and required drainage. The extravasation probably is responsible for most instances of perinephritis and perinephric abscesses rather than direct ruptures of cortical abscesses. It also accounts for some cases of fibrolipomatosis of the renal sinus, localized retroperitoneal fibrosis and, occasionally, strictures of the upper ureter and calyceal infundibula. In episodes of ureteral obstruction, the associated fever and leukocytosis are often due to extravasation when urinary tract infection is absent.

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SPONTANEOUS RUPTURE OF THE RENAL PELVIS*

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MUCH has been written in the radiologic and urologic literature about the various "backflow" phenomena associated with obstruction of the upper urinary tract. 1,6,7,13,15,18,19,25,26 Very little has been published in the radiologic literature concerning a type of backflow which is due to a spontaneous rupture of the renal pelvis secondary to urinary tract obstruction. The urologic literature has recognized spontaneous rupture in the past. 2,3,4,5,9,12,14,20,21,22,23,27,28

Wunderlich²⁹ in 1856 is credited with being the first to describe "spontaneous apoplexy of the renal capsule." Shaw,27 in his recent review of 40 cases of nontraumatic renal rupture, could only find 3 cases occurring in previously normal kidneys. In fact, several authors state that pre-existing disease is a necessity for rupture: hydronephrosis, tuberculosis, lithiasis, tumors, or severe trauma. Weiner et al.28 described a case with findings on intravenous pyelography similar to those of our patients. They used abdominal compression, however, and, therefore, their case was not conclusive. All of our patients were examined without abdominal compression. Weiner and co-workers' study also showed the "white stripe" of contrast material along the upper psoas border to be referred to later on.

Pyelolymphatic backflow has been extensively studied by Ollson, ^{10,19} Narath ^{15,16} and Lindbom. ¹³ Their opinion is that pyelorenal backflow is due to a rupture at the fornical angle near one of the calyces. From this point, contrast material can assume several contours.

Over the past 4 years we have had the opportunity of studying 4 cases which would indicate to us that the entity of so-called "pyelointerstitial backflow" is in

certain instances due to actual rupture of the renal pelvis.

REPORT OF CASES

Case I. B. M., a 45 year old male, entered the hospital with classic complaints of right renal colic of several hours' duration. Past history was noncontributory. After clinical evaluation intravenous urography was performed (Fig. 1, A-C). A scout film showed an intact psoas margin on the right and gallstones. No ureteral concrements were visible. No abnormality of the left kidney and ureter was demonstrated after the injection of contrast material. On the right, a nephrogram appeared on the 15 minute film. On the 60 minute film (Fig. 1B), it was evident that the nephrogram was clearing, but that the psoas margin had become obliterated during the same interval. On the 2 hour film (Fig. 1C), contrast material was seen streaking down the right psoas muscle margin. At the time that the 60 minute study was being made, the patient volunteered the information that his back pain had gone and his only current discomfort was a dull abdominal ache.

A diagnosis of retroperitoneal rupture was made by means of the intravenous urogram. The patient was brought to cystoscopy and a No. 5 ureteral catheter passed. A retrograde injection of contrast material added to the contrast already present in the retroperitoneum (Fig. 1D). The next morning he was operated upon and a spiculated uric acid stone was removed from the intramural end of the right ureter. Retroperitoneal exploration revealed urine and edema fluid. Recovery was rapid and uncomplicated. All urine cultures were persistently sterile. An intravenous pyelogram 3 months later was entirely normal (Fig. 1E).

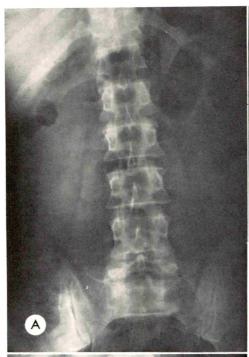
Case II. H. N., a 70 year old female, was admitted to the surgical service with a 3 day history of left lower quadrant abdominal pain. The pain was accompanied by nausea, bloating, and abdominal distention. The patient had had

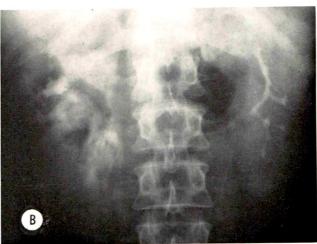
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no bowel movements during the interval. The initial clinical impression was acute diverticulitis and because of this an emergency barium enema study was performed. This examination was normal. A urinalysis showed a few red and white blood cells, but was otherwise unremarkable. In view of the past history of 2 or 3 lower urinary tract infections, intravenous urography was subsequently performed (Fig. 2, A and B). This was followed by cystoscopy and left retrograde urography. A small obstructing calculus

in the lower end of the left ureter could not be removed from below; however, it was dislodged from its position allowing relief of the hydroureter and hydronephrosis. Re-examination 2 weeks subsequent to this (Fig. 2C) showed some residual hydronephrosis and hydroureter with retention of the calculus. The patient was, at this time, asymptomatic and there was no evidence of extravasation.

CASE III. W. M., a 56 year old male, was seen





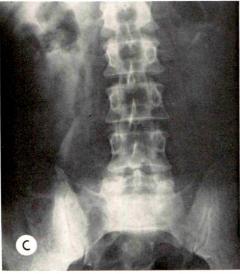
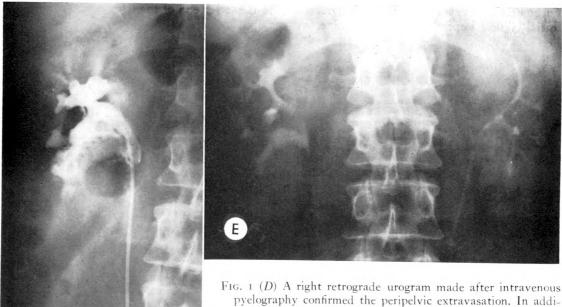


Fig. 1. Case 1. (A) Scout roentgenogram prior to injection for intravenous pyelography. Note well delineated right psoas border. (B) Sixty minute pyelogram showing obliteration of upper one-third of right psoas border and peripelvic extravasation of contrast material. (C) Two hour pyelogram. Note complete obliteration of the psoas border and dissection of urine and contrast material along psoas border. Note "white stripe" just above the right iliac bone produced by the extravasated contrast material dissecting in the retroperitoneal tissues.



pyelography confirmed the peripelvic extravasation. In addition there appears to be the usual pyelorenal backflow seen in association with overdistention of the renal pelvis in retrograde urography. Note contrast material adjacent to psoas margin from prior intravenous pyelography. This shows why an intra-

venous urogram, as the initial study, is essential in demonstrating spontaneous rupture. (E) Follow-up study 3 months later shows return to normal of the right collecting system following surgical exploration and removal of the ureteral calculus.

in the Emergency Room with a 48 hour history of vague left upper quadrant pain increasing in severity, but without radiation. There were no direct urinary symptoms. The urinalysis showed 15 red blood cells and 17 white blood cells per high power field. An emergency intravenous pyelography was performed (Fig. 3, A and B), after which an obstructing calculus in the lower end of the left ureter was removed by means of a ureteral basket and a No. 7 ureteral catheter was placed in the left renal pelvis where it was left for 48 hours. An intravenous urogram made 4 days subsequent to this was entirely normal (Fig. 3C).

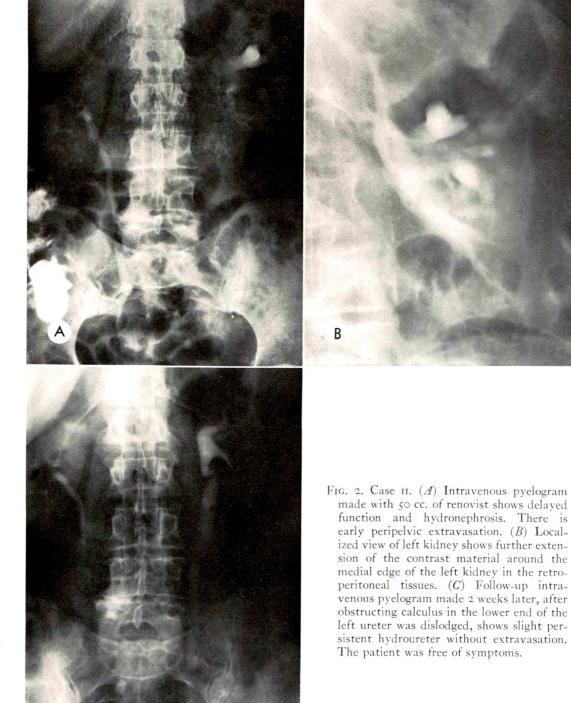
Case IV. G. Y., a 58 year old female, presented with a 2 week history of right sided costovertebral angle pain radiating to the right groin. There were no other urinary complaints. Pelvic examination showed a fixed mass in the retroperitoneal area of the right side of the pelvis enveloping the right ureter and invading the broad ligament. A biopsy of the mass revealed reticulum cell sarcoma (Fig. 4, A,B and C).

The possibility that the patient passed a tiny

calculus with initial acute obstruction superimposed on the more chronic obstruction due to the pelvic mass cannot be entirely excluded.

Comment. We refer to the findings in our patients as "spontaneous pelvic rupture" rather than pyelointerstitial backflow. The fact that the patient symptomatology and the pyelographic picture change dramatically with extravasation indicates that true rupture does occur. The pattern of extravasation is different from pyelointerstitial backflow and there is evidence of extension into the retroperitoneal space. For these reasons we believe that in all our patients actual spontaneous rupture occurred in contradistinction to the opinion of Serebro et al.²⁶ who maintain that extravasation occurs without rupture.

This was confirmed by the operative finding of retroperitoneal urine in Case I and the rapid return to normal in Cases II and III, once the obstruction had been released. Our studies show that in 3 out of the



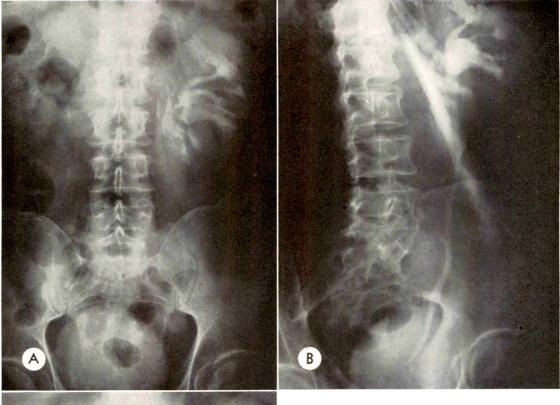




Fig. 3. Case III. (A) Intravenous pyelogram, made during acute attack of renal colic with 50 cc. of renovist, shows early extravasation as well as faint "negative" defect of nonopaque ureter within the dense contrast along the upper psoas border. This is one of the later studies. Note that the contrast material has almost completely disappeared from the normal right kidney. (B) Delayed intravenous pyelogram shows marked extension of extravasated contrast material along the entire psoas border. Note the "white stripe" of contrast material dissecting along the psoas border in the retroperitoneal tissues. This appearance would be pathognomonic for this entity. (C) Follow-up intravenous pyelogram a few days after removal of obstructing calculus in the lower end of the left ureter shows return to normal.

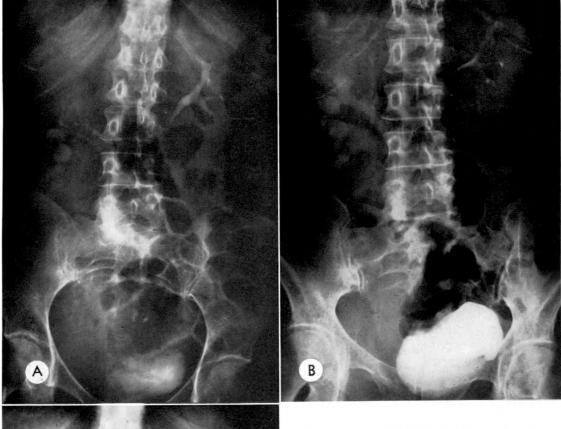




Fig. 4. Case iv. (A) Early intravenous pyelogram with 50 cc. of renovist made during episode of right flank pain shows early extravasation of the contrast material in the periureteral tissue around the upper ureter draining the upper collecting system. As noted, the patient has a double collecting system. Notice negative outline of ureter in contrast material. A large right sided pelvic mass indents the right side of the bladder. (B) One-half hour pyelogram shows further extension of extravasation. The ureter to the upper calyces is now outlined with contrast material and separated by the non-opaque wall of the ureter from the extravasated material. The extravasated contrast material also outlines the upper end of the second ureter at this time. (C) Follow-up study a few days later, after subsidence of acute renal colic type symptoms and before roentgen-ray treatment was initiated. The study no longer shows the extravasation. There is persistence of hydronephrosis and hydroureter of the double collecting system, most likely produced by the pelvic mass. This would be a situation of pre-existing disease.

4 patients we were dealing with originally normal kidneys as well. The work of Hinman, and Hamperl and Dallenbach would also indicate this. Three of our cases which had a calculus in the lower ureter were studied while clinical renal colic was present. Two of the patients had a profound change of clinical symptomatology during the course of their disease. Before rupture, the symptoms of renal colic were outstanding; with rupture the colicky pain disappeared and abdominal pain supervened. In all cases a prolonged nephrographic effect indicated increased intrarenal pressure.

In Cases II and III, the obstructive cause was removed and a normal intravenous pyelogram was obtained shortly thereafter. Cases I and III showed opaque material outlining the retroperitoneal structures as well as periureteral extravasation. The contrast material outlining the psoas borders can be visualized on the roentgenogram. We refer to this as a "white stripe."

The first patient was examined during the actual occurrence of pelvic rupture and, therefore, provided a unique opportunity to study the development of the rupture roentgenographically. The patient underwent ureteral and a retroperitoneal surgical exploration subsequent to intravenous and retrograde pyelography. A ureteral calculus was recovered and urine was found dissecting retroperitoneal tissue planes.

In all cases extravasation of contrast material occurred without the use of extrinsic abdominal compression or any other type of instrumentation and was first demonstrated by means of intravenous urography.

DISCUSSION

Diagnosis of an acute rupture by intravenous pyelography in an otherwise normal kidney is rare, with only a few cases having been diagnosed preoperatively.

Shaw²⁷ reviewed 40 cases of nontraumatic renal rupture and could find but 3 occurring in previously normal kidneys. He found that the greatest cause of rupture

was hydronephrosis and 72 per cent of his cases showed this. Most of these hydrone-phrotic kidneys were secondary to stone formation and ensuing obstruction. Most of the cases of rupture were males (32:8) and the right kidney was ruptured more frequently than the left (24:15). In I case bilateral rupture occurred.

After the study of our cases, we believe that the following sequence of events takes place:

- 1. There is a delay in excretion of contrast material as is usually the case in obstructive uropathy with associated stasis.
 - 2. A nephrogram phase appears.
- 3. Rupture of the renal pelvis occurs. The increased pressure is released and the urine containing contrast material passes from the tubules into the calyces and pelvis. With this, the nephrogram disappears. In Case I, in which the rupture occurred during the examination, the nephrographic phase lasted for less than 45 minutes.
- 4. Contrast material is then seen leaving the confines of the renal collecting system, dispersing into the retroperitoneal tissues. The first indication of this will be loss of definition of the psoas muscle shadow adjacent to the renal pelvis. This is due to loss of fat density as the peripelvic fat is infiltrated with urine and edema fluid.
- 5. Clearly confined streaks of contrast material are seen collecting along the psoas muscle. The density of this extravasated medium will depend on the timing of the roentgenographic study but its appearance will clearly establish the diagnosis.

If the examination is done early in the course of the disease, there will be good concentration of the contrast material, but if done late, the contrast material will be rapidly diluted by urine and retroperitoneal edema fluid. We found that it took less than 6 hours to dilute the contrast material to a density close to that of water. A roentgenogram made 6 hours after retrograde pyelography showed only retroperitoneal edema in our first case.

It is often helpful to pay careful attention to the lower pole of the kidney shadow

since contrast material often pools in this area as gravity dictates.

The cause for the extravasation appears to be the increased hydrostatic pressure in the ureter secondary to the obstruction.

CONCLUSION

Four cases of spontaneous rupture of the renal pelvis are reported with roentgenographic documentation of the chain of events, during rupture and recovery.

It is our opinion that we are dealing with a true rupture due to sudden increase in pressure in the pelvoureteral space.

Rupture probably occurs at the point of least resistance, the fornix.

Rupture is most often associated with a calculus in the ureter, but may occur with other forms of obstruction, e.g., tumor,

There may be no evidence of pre-existing kidney disease; rupture can occur in otherwise normal kidneys.

There well can be a change in the symptom pattern the patient describes, or in the clinical findings after rupture occurs.

Rupture, although a potentially serious complication of an acutely obstructing ureteral calculus, can be easily recognized and should be properly interpreted. No immediate surgery is indicated on the kidney. The goal should be removal of the cause of obstruction. Removal of the calculus and catheter drainage for 24 hours may be sufficient.

The use of larger volumes of more concentrated opaque materials for intravenous urography is recommended.

Intravenous urography should be the first diagnostic study in order to remove the possibility of iatrogenic rupture of the renal pelvis during retrograde urography.

SUMMARY

Four cases of spontaneous rupture of renal pelves, demonstrated by intravenous pyelography and proven by operative findings and follow-up studies, are reported and discussed.

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SUBTOTAL RENAL INFARCTIONS*

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ALTHOUGH subtotal renal infarction is not uncommon, the diagnosis is seldom made clinically. Most of the descriptions of renal infarcts have been made at autopsy. Barney and Mintz in 1933 (as quoted by Regan and Crabtree⁶) described 143 autopsy cases of renal infarctions and noted that the diagnosis had not been made clinically in any of them. In 205 cases of renal infarction described at autopsy, Hoxie and Coggin³ found that the diagnosis was made in only 2 of the cases. Regan and Crabtree⁶ in 1948 reviewed the subject thoroughly, deplored the lack of clinical acuteness in making the diagnosis of renal infarction, and developed the guide lines for the diagnosis. In 94 patients, renal infarctions were divided into 3 categories, consisting of arterial infarction, venous infarction, and traumatic infarction. They pointed out that the clinical diagnosis of arterial infarction rested on the following points: sudden onset of pain in the flank or upper abdomen, the demonstration by intravenous pyelogram of a nonfunctioning kidney on the involved side, the finding on retrograde pyelogram of a normal collecting system and ureter, albuminuria and either gross or microscopic hematuria, unilateral alteration in renal function studies, and the associated presence of cardiac or vascular disease. They reported only 3 cases of traumatic infarction and stated that they are quite rare. In 1958, Mulholland⁵ reported on the successful utilization of renal arteriography to confirm the diagnosis of renal infarction. In a more recent article, Janower and Weber⁴ also stress the importance of contrast visualization of the renal arteries in the diagnosis of renal infarction. In 1961, Heitzman and Perchik² pointed out that small segmental infarcts may either produce no intravenous pyelographic abnormality or cause local failure of calyceal filling. In the same year, Haynie and associates,¹ utilizing the renal isotope scintiscan, described the usefulness of this modality in detecting ischemia and localized infarcted areas in the kidney. They showed that segmental infarcts as small as 3 cm. by 2 cm. could be detected, and correctly predicted the operative findings in 80 per cent of the cases. Since scintiscanning has become available, the diagnosis of subtotal renal infarcts can be made more often and has prompted this report of our experiences.

MATERIAL

We reviewed 218 renal scans performed since October, 1962. Among this material we had 10 cases of subtotal renal infarction. Two cases were secondary to embolic phenomenon in patients with rheumatic mitral valve disease and auricular fibrillation. Three cases were thought to be the direct result of trauma. Two were due to dissecting aneurysm which involved secondary branches of the renal artery. One case resulted from arteriosclerotic changes in the renal artery, and in 2 patients the diagnosis was made without evidence of a causative factor. An additional case mimicked in all respects a segmental infarction. This was later found at surgery to be the result of a tuberculous obliterative endarteritis with abscess formation.

ILLUSTRATIVE CASES

Case I. M.G. was a 44 year old woman with rheumatic heart disease, mitral stenosis, and auricular fibrillation who entered the hospital in January, 1963, with right lower quadrant abdominal and flank pain. She was afebrile. Some costovertebral angle tenderness was noted on the right. Six urinalyses failed to disclose any gross or microscopic hematuria. A slight leuko-

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cytosis was present. On February 4, 1963, intravenous pyelography was performed which was essentially normal. The next day a retrograde examination was found to be negative (Fig. 1 and 2).

Because of the continued abdominal pain, surgical exploration was then carried out. This failed to reveal any definite abnormal finding. The pain subsided somewhat, and 10 days later a renal isotope scan (Fig. 3) showed a discrete area of nonfunction, representing an infarct.

Comment. This case demonstrates how misleading clinical and laboratory findings may be in the case of subtotal infarction. It also emphasizes the ease and accuracy with which the diagnosis can be made by renal scanning if this modality is considered.

Case II. A.O., a 53 year old patient with a known history of rheumatic heart disease, had pain in the left flank associated with microscopic hematuria. The intravenous and retrograde pyelograms (Fig. 4 and 5) showed poor filling of the middle calyx of the left kidney. The renal scan showed a well defined defect in the center of the kidney (Fig. 6).

Comment. The well recognized sign of absence of change in the retrograde pyelogram in arterial infarction did not obtain



Fig. 1. Case 1. Intravenous pyelogram obtained February 4, 1963, has a normal appearance.



Fig. 2. Case i. Retrograde pyelogram on February 5, 1963, is also negative.

here. The defect noted on the intravenous and retrograde pyelogram was probably due to edema surrounding the infarct. The renal scan clearly demonstrated the infarcted area.

Case III. E.H. was a 20 year old male who injured the left side of his abdomen and developed hematuria in October, 1963. An intravenous pyelogram on the same day demonstrated poor filling of the left middle calyx and a narrow infundibulum (Fig. 7). The renal scan showed a central defect, indicating a traumatic infarct

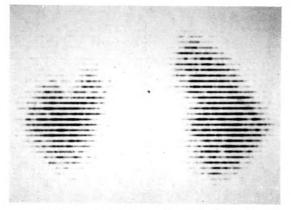


Fig. 3. Case I. Renal scan obtained February 15, 1963, demonstrates a discrete area of nonfunction in the superior pole of the right kidney.



Fig. 4. Case II. Nonvisualization of the middle calyceal group on intravenous pyelogram.

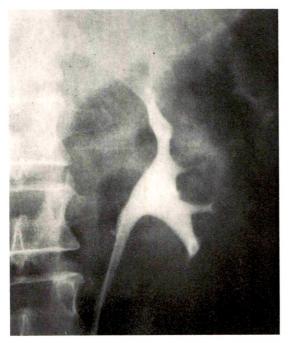


Fig. 5. Case II. Attenuation in caliber of the infundibular aspect of the middle calyx on retrograde study.

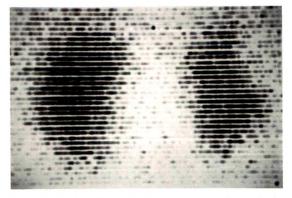


Fig. 6. Case II. Scan discloses absence of uptake in the area corresponding to the middle calyceal distribution.

(Fig. 8). A follow-up examination 6 months later showed a negative intravenous pyelogram, but a persisting area of nonfunction was seen on the renal scan.

Comment. In this case, as in the last, the surrounding edema or hemorrhage associated with a subtotal infarct altered the intravenous pyelogram in the acute phase. This later was found to return to a more normal appearance. The scan demonstrated the lesion long after it became asymptomatic. This may have some significance in



Fig. 7. Case III. Poor calyceal filling throughout the kidney. The middle calyceal group is not visualized.

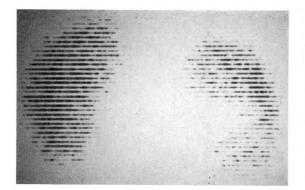


Fig. 8. Case III. Large central scan defect.

medicolegal applications as well as in the investigation of a renal basis for the later development of hypertension following renal injury and arterial damage.

Case IV. R.P. injured his right side 3 weeks prior to admission to the hospital. He was admitted with fever and pain in the right flank. Urine examination was entirely negative. A slight leukocytosis was present. The intravenous pyelogram (Fig. 9) showed fullness of the upper pole of the right kidney which raised the question of a mass or bifid kidney. There was no distortion of the visible calyces. The renal



Fig. 9. Case IV. Intravenous pyelogram showing enlargement of the superior pole of the right kidney.

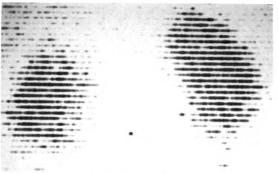


Fig. 10. Case IV. Absence of function in the region of the superior pole enlargement.

scan (Fig. 10) revealed absent function of the upper pole. At surgery, an area of infarction was encountered in the upper pole of the kidney as well as a small adjacent subcapsular abscess.

Comment. The renal scan was instrumental in influencing early surgical exploration.

Case v. J.P. fractured a left rib in an automobile accident in June, 1963. Following the accident, the patient experienced intermittent hematuria. When studied 6 months later, an intravenous pyelogram was thought to be normal. A scan defect was demonstrated in the lower pole of his left kidney (Fig. 11). A translumbar aortogram demonstrated absence of arterial blood supply to the lower pole of the involved kidney (Fig. 12).

Comment. Despite a normal intravenous pyelogram 6 months following trauma, the renal scan clearly defined a segmental area



Fig. 11. Case v. Large scan defect in the lower pole of the left kidney.



Fig. 12. Case v. Translumbar aortogram demonstrating decreased arterial supply to the lower pole of the left kidney.

of deficient blood supply which was confirmed by arteriographic study.

Case VI. A 30 year old physician presented with obscure abdominal pain. He was also found to be hypertensive. Two of 5 urinalyses revealed a small number of red blood cells. An intravenous pyelogram (Fig. 13) showed minimal dilatation of the upper calyces of the right



Fig. 13. Case vi. Dilatation of the minor calyces in the superior pole of the right kidney.

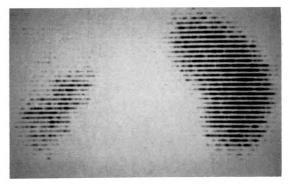


Fig. 14. Case vi. Absent function in the upper pole of the right kidney.

kidney. The renal scan (Fig. 14) showed no function in the upper pole of the right kidney. A percutaneous femoral aortogram (Fig. 15) demonstrated atherosclerosis of the lower aorta associated with renal artery stenosis and avascularity of the upper pole of the right kidney. At surgery, the upper pole of the right kidney was found to be infarcted and was surgically removed.

Comment. Obscure abdominal pain with meager urine findings and pyelographic findings almost prompted an abdominal exploratory operation in this patient. Although aortography was contemplated in

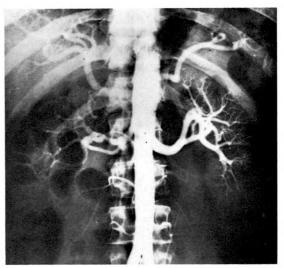


Fig. 15. Case vi. Percutaneous femoral aortogram demonstrates stenosis of the right renal artery, poststenotic dilatation, aneurysm of the main artery, and avascularity of the upper half of the kidney.

the future to further investigate the patient's hypertension, the renal scan enabled us to quickly localize the basis of the abdominal pain.

Case VII and VIII. Two patients with dissecting aneurysm and left flank pain were seen. In one, the intravenous pyelogram showed some diminished function of the left kidney and a scan showed a well defined defect. The aortogram demonstrated dissection of the aorta involving the left main renal artery with occlusion of some of its secondary branches. In the second case, the intravenous pyelogram showed no filling of the middle calyx. On the renal scan an upper pole defect was evident.

Two other patients with subtotal renal infarctions of undetermined etiology were seen. In one, a 30 year old male, cramping abdominal pain was present. The urine examination was negative. An intravenous pyelogram was normal. The scan showed a distinct subtotal infarct which came as quite a surprise to the clinicians. Aortography was not carried out on this patient.

DISCUSSION

Cardiac disease accounted for only 2 of our cases of renal infarction in contrast to the high percentage in published reports. The high incidence of diagnosed traumatic infarcts in this group is surprising and is probably due to the sensitivity of the scintiscan in detecting them.

The commonly presented clinical and roentgenographic criteria described in the case of major renal artery occlusion with infarction are not applicable in the diagnosis of smaller subtotal infarcts. Pain, often abdominal in location and colicky in nature, may simulate a surgical abdomen and prompt needless exploration. In other instances paucity of clinical and laboratory findings may delay diagnosis and result in a lengthy and costly hospital stay.

Findings on urinalysis are quite variable with the examination often disclosing no red blood cells in the urine. Albuminuria has been reported to occur in the majority of cases.⁴

The pyelographic changes are related to

the age and the extent of the lesion. Nonfunction of a kidney is generally associated with occlusion of a main renal artery although segmental occlusion can result in absence of visualization of the collecting system.4 Localized alteration in excretion and anatomic detail occurred in 8 of our patients. In 4 cases, the changes were minimal with lack of filling or distortion of one or two minor calyces being evident. In 1 case there was generalized diminished function. A follow-up intravenous pyelogram obtained on one of the patients with a traumatic infarct who initially showed both a scan defect and an alteration of a calyx on intravenous pyelography demonstrated a return to normal. This led us to believe that the early pyelographic changes were due to transient edema on the margins of the infarct. Some months after an acute infarction, I case showed localized loss of cortical substance and another showed blunting of two minor calyces.

The ease with which the renal scan can be done makes this a valuable diagnostic method in evaluating possible subtotal infarctions. The defects on the scan must be correlated with the intravenous pyelogram and, at times, with contrast study of the renal arteries. It cannot be used alone since abscesses, tumors, cysts, and localized obstruction with nonfunction of a segment of the kidney may also cause a similar appearance. Atrophy or hypoplasia of the kidney can cause a diminished renal outline that resembles an end pole infarct. However, in the case of subtotal infarction, the diagnosis becomes more obvious when one superimposes the scan on the intravenous pyelogram and finds the soft tissue renal outline larger than the functioning area demonstrated on the scan. Cystic degeneration or infection of an infarct with abscess formation may cause distortion of the calyces which makes the diagnosis at times uncertain. In each case when a renal scan was obtained in both the early and late stages of infarction, a defect was detected. Bilateral infarctions or small ones, if present, were not detected.

The renal arteriogram was useful in determining the underlying etiology. Aortography was performed in 4 of our cases and in each instance confirmed the avascularity of a lesion demonstrated on the scan. In one instance, unexpected atheromatous changes were demonstrated in a young man. In another case, aortography revealed a dissecting aneurysm blocking a renal artery.

SUMMARY AND CONCLUSIONS

Our experience with 10 cases of subtotal renal infarctions has been reviewed. The clinical and laboratory picture of subtotal infarct is quite variable and often misleading. The clinician must rely almost entirely upon radiologic procedures to establish the diagnosis. The roentgen findings in subtotal infarct differ from total infarct but have not been found to be characteristic. The renal scintiscan has proved to be a reliable method in the detection of subtotal infarctions when correlated with other radiographic studies. Aortography is necessary to localize the arterial occlusion and to demonstrate underlying pathology. The occurrence of traumatic subtotal infarction is not as uncommon as the literature would

indicate. More frequent detection of traumatic subtotal infarcts will result from a high index of suspicion and the utilization of renal isotope scanning in cases of renal trauma.

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RENAL INFARCT WITH PERIRENAL HEMATOMA*

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THE interest of the reported case lies in the fact that a partial renal infarct, complicated by an important perirenal hematoma, occurred in a patient under investigation without any clinical manifestation. Moreover, it was possible to obtain an angiographic and surgical study of this lesion. Uson et al.²⁴ have already mentioned the clinical silence of such lesions. This case is presented in order to confirm this fact and stress the importance of the roentgenologic signs for the diagnosis.

REPORT OF A CASE

A 40 year old white male was admitted to Notre Dame Hospital for investigation and evaluation of arterial hypertension, diagnosed recently in the course of a pre-employment physical examination.

Subjective History. For the past 8 years, the patient had noted a decrease in strength in the upper and lower right extremities. He also complained of nocturnal right calf pain. For the last 5 years, he had noticed a progressive exertional dyspnea, but no anginal pain, no headache and no vertigo. Except for profuse sudation, the rest of the history was essentially negative.

Physical Examination. This showed a hypertensive retinitis, Grade 3/4, astigmatism and some exudates in the right eye. The lung evaluation was normal. The heart auscultation revealed a mesocardiac systolic murmur, Grade 2/4. The arterial blood pressure was 240/140 mm. Hg at the upper limbs and 260/150 mm. Hg at the lower limbs, on decubitus. The abdominal examination showed no mass or pain on palpation.

Laboratory Findings. Blood and urine examination yielded essentially normal values: the blood urea nitrogen was 36 mg. per cent, the sedimentation rate 6 mm./1 hour. Complete blood count, differential count and urinalysis were normal. Electrolytes were as follows: blood calcium 9.6 mg. per cent; Cl 100.5 mEq/l and Na 147 mEq/l.

The electrocardiogram showed signs of myocardial ischemia. Total cholesterol was 169 mg. per cent, esthers 65 per cent, bromsulphalein 70 per cent (2 hours), acid phosphatase I unit, and phenolsulfonphthalein 26 per cent (15 minutes).

The special studies for arterial hypertension included: V.M.A. 4.1 ml./24 hours (normal), regitine test negative, and Stamey test (differential renal function) normal.

Roentgenologic Examination. Admission chest roentgenograms did not show any costal erosion, or a pleuroparenchymal lesion. There seemed to be a slight increase in total heart volume, possibly due to enlargement of the left ventricle. The cardio-thoracic ratio was 16.5/31. There was marked elongation of the thoracic aorta, without visible calcifications in the wall.

Renal pathology was considered next and intravenous pyelography was done a few days later. The examination revealed symmetrically appearing nephrograms followed by simultaneous pyelocalyceal opacification. A small pyelogenic cyst was present in the upper part of the left kidney. The bipolar diameter of the right kidney was 14 cm. and of the left kidney 13 cm. The renal outlines were smooth and regular (Fig. 1). The psoas muscles were normal in appearance.

Renal angiography was accomplished by the percutaneous transfemoral method, using a yellow Ödman, Kifa catheter, placed 20 inches in the aorta opposite L2. After an initial 10 cc. injection of renografin 76 per cent (methylglucamine diatrizoate) for verification purposes, 35 cc. of renografin 76 per cent was injected in 1 to 1.5 seconds. Anteroposterior roentgenograms were taken at the rate of 2 per second. In order to obtain a more adequate evaluation of the renal artery take-off, the procedure was repeated after rotating the patient, thus obtaining a slightly oblique view with the colon displaced away from the right kidney.

The examination demonstrated a tortuous aorta but no notching or atheromatous plaques. The bipolar orientation of the right kidney was

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Fig. 1. The intravenous pyelogram shows a normal right renal outline.

almost vertical, representing a change of position from that noted on the recent intravenous pyelogram. Two renal arteries were visible on each side. The take-off of the right renal arteries overlapped each other. The superior right renal artery supplied the upper third and part of the middle third of the kidney, whereas the inferior artery supplied the rest of the kidney. A discrete narrowing immediately above the short trunk of this inferior artery could not be eliminated entirely.

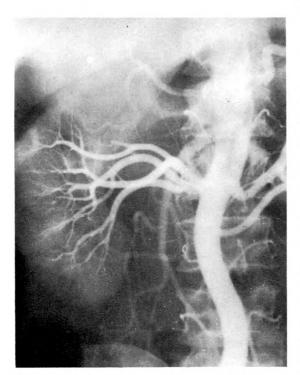


Fig. 2. Arterial phase of aortogram showing an occluded branch of the renal artery and an abnormally dense suprarenal shadow.

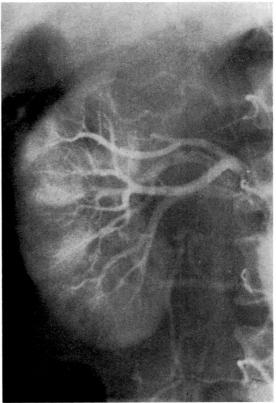


Fig. 3. Close-up of the lesion with more advanced arterial filling.

A complete obstruction of one of the secondary branches of the superior renal artery was noted (Fig. 2 and 3). No nephrogram was seen in the corresponding segment of the upper pole of the kidney. A large round mass was noted adjacent to that kidney area, containing no contrast medium or calcification and measuring 8×9 cm.

Comment on Angiography. The aortography revealed a mass that was not demonstrated or that did not exist at the time of the previous roentgenography. This mass, with a round inferior outline, situated opposite the superior pole of the right kidney, could very well have been associated with some neighboring organ: adrenal, liver, etc. However, other angiographic findings, such as the absence of a nephrogram in a well defined sector affecting a vaguely triangular shape at the upper pole of the right kidney (Fig. 4) and, above all, the obliteration of a secondary branch of the superior right renal artery were suggestive of a renal infarct. An adrenal tumor would not impair the vascu-

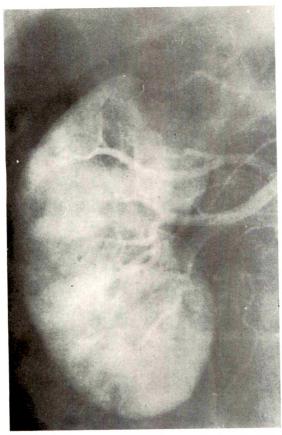


Fig. 4. Nephrographic phase shows absence of filling at the upper pole.

lar supply of a kidney unless some malignant invasion were present. The absence of opacification of abnormal vessels in this area did not favor this possibility.

Periarteritis nodosa is one of the causes of perirenal hematoma but the roentgenologic diagnosis must depend to a greater extent on clinical contribution. If ectasias of fine intrarenal arteries associated with perirenal hematoma are found, this pathology might be one to be considered.

A perusal of the literature revealed a rarity of angiographic studies demonstrating a perirenal hematoma with renal infarct. Nevertheless, some investigators 5.6.10,12,14,19,20,23 reported angiographic findings pertinent to those in the presently reported case (Fig. 3 and 4), together with discussion of the differential diagnosis.

Surgical Findings. The patient was explored surgically to determine the nature of the suprarenal mass and to evaluate the renal artery for possible stenosis. He was placed in decubitus

position and the abdomen was prepared and draped in the usual fashion in order to permit a right Kocher incision. The intra-abdominal exploration was negative. The posterior peritoneum was incised along the lateral border of the second portion of the duodenum. The incision was extended laterally to the hepatic flexure. The right renal pedicle was identified and the intraluminal pressure of the arteries was taken but no significant gradient was registered within the aorta. The mass was explored next. As the kidney was being freed from the perirenal fat, the mass was visualized. It was gray, hemorrhagic, firm, and adherent to the kidney and to the perirenal (Gerota) fascia. Because hypernephroma was a possibility, a Satinsky clamp was placed on the renal pedicle and a heminephrectomy was done, removing the adherent mass and staying well within normal tissue throughout. The kidney was closed in the usual manner and the pedicle clamp was re-

Section of the specimen revealed a renal infarct with hematoma adherent to the base of



Fig. 5. Operative specimen showing the resected upper pole of the kidney with a triangular infarcted area and the large fresh hematoma on top.



Fig. 6. Close-up of the resected surgical specimen showing the triangular infarcted area and the thrombosed vein (arrow) and artery (double arrow).

the pyramid and extending to the perirenal fat (Fig. 5 and 6).

The convalescence was uneventful except for a drop of the hemoglobin which was readily corrected with 1,000 cc. of whole blood.

The blood pressure remained constant throughout the hospital stay but no beneficial effect on the arterial hypertension could be observed following the accomplished surgical procedure.

The patient was seen a year later, at which time an intravenous pyelogram was normal. The right kidney showed the expected decrease in size from the previous surgery (Fig. 7).

Pathologic Findings. The renal infarct showed total necrosis with some ghost renal structures. Granulation tissue was present at the edges of the lesion. At the apex of the infarct, the apical arteries showed thrombosis of two ages: old, recanalized and fibrosed; and recent and invaded by endothelial cells and macrophages (probable age: 10–15 days). The thrombus was

partially revascularized by a large sinus lined by hyperplastic endothelium (probable age: 10-15 days).

The wall of the hematoma was composed of highly vascularized granulation tissue, rich in macrophages full of hemosiderin, lymphocytes and plasmocytes. Here and there were islets of erythropoiesis. The granulation tissue was approximately 15 days old.

Outside the infarct, the interlobar and interlobular arteries presented subintimal lamellar sclerosis which reduced their lumen by one-third. Hyalin degeneration was observed at the site of the afferent arteries.

The pathologic diagnosis was: renal arteriosclerosis, renal infarct, old thrombosis of a secondary artery, recent thrombosis of a secondary artery and vein and recent perirenal hematoma.

DISCUSSION RENAL INFARCT

An infarct is a zone of ischemic necrosis secondary to the sudden occlusion of a vein or an artery. It is one of the most common vascular nephropathies. The greater vulnerability of the left kidney is attributed to its longer pedicle. The renal circulation is terminal in type, thus favoring infarcts.

Two elements tend to aggravate this lesion: infection and the venous origin. In children, according to Kaufman, 60 per

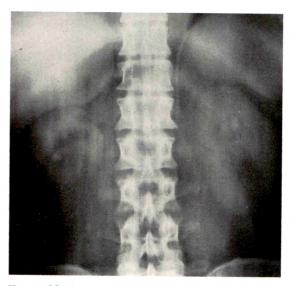


Fig. 7. Nephrotomogram, 14 months following surgery, showing a normally functioning right kidney.

cent occur during the first month of life.

The infarct may be arterial or ischemic, which differentiates it from glomerular nephropathy (Osler's disease), bilateral cortical necrosis due to an acute capillary vasomotor dysfunction and Moschowitz' thrombotic micro-angiopathies,18 or it may be venous or hemorrhagic. The sudden and complete occlusion of the vein is necessary to produce an infarct; a partial or progressive lesion does not produce an infarct. In children, thrombosis of a renal vein is often a complication of a debilitating condition. It is said to be fatal in 90 per cent of the cases. Finally, an infarct may be traumatic, that is, secondary to a renal pedicle contusion from trauma or surgery.13

PERIRENAL HEMATOMA

Three names stand out in the historical survey of perirenal hematoma. Bonet, in 1700, reported the first case. Wunderlich, in 1856, is credited with the original classic description of the lesion and Lenke, in 1909, described the triad of clinical symptoms, to which have been added lumbar pain, flank mass and signs of internal hemorrhage. The clinical facets have been further studied by others.²⁴

Surprisingly, the cause of perirenal hematoma is unknown in about 15 per cent of the cases. Among the known causes are: (1) renal pathology; (2) injury or hemorrhage of neighboring organs; and (3) hemorrhage in systemic diseases.

(1) Renal pathology is responsible for many cases. In this group are: (a) renal trauma of variable intensity which may obviously cause hematoma. Thus, the history of trauma, especially in atheletes, is diagnostic; (b) trauma from renal biopsy or retrograde pyelography; (c) renal neoplasm; 21,22 (d) nephritis; (e) tuberculosis; (f) kidney rupture, which is always accompanied by a hematoma whether secondary to cysts, polycystic disease, neoplasm or hydronephrosis complicated by pyelonephritis. The mechanism responsible for these ruptures would be increased abdominal pressure such as that occurring during

delivery;¹⁵ (g) nephrolithiasis; (h) renal infarct.² In 76–95 per cent of cases, this is attributed to a cardiopathy:¹³ myocardial infarct, endocarditis, mitral stenosis with fibrillation, intra-auricular thrombosis, congenital cardiopathies; (i) endarteritis of the renal artery; (j) rupture of the renal artery aneurysm as well as retroperitoneal surgery to large vessels; and (k) fibromuscular hyperplasia of the renal artery might be considered a possible cause of hematoma if rupture occurred in the zones of deficiency in the media. However, to our knowledge no such case has yet been reported.

(2) Neighboring organs or structures may be responsible for perirenal hematoma in the following situations: (a) lumbar trauma with or without fracture; (b) obstetrical trauma to the adrenal; (c) rupture of an aortic aneurysm; (d) perirenal lipomas; and (e) perirenal mesothelioma.

(3) Lastly, systemic diseases are capable of producing perirenal hematoma. These include: (a) acute infections; (b) periarteritis nodosa with the usually bilateral kidney involvement; (c) leukosis; (d) blood dyscrasias: hemophilia, thrombocytopenic purpura, polycythemia; (e) lupus erythematosus; (f) arteriosclerosis; and (g) anticoagulant therapy.

According to Presman et al.²¹ perirenal hematomas may be situated in the subcapsular region, thus explaining the sudden elevation of blood pressure. Engel and Page⁷ liken this phenomenon to that of the "cellophane kidney" produced in rats. These hematomas may also occur between the capsule and Gerota's fascia, or outside Gerota's fascia in the peritoneal cavity.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The renal infarct with a perirenal hematoma is characterized clinically by the site where it is produced and the caliber of the obliterated vessel. ²⁴ In the dramatic type, one should look for Lenke's triad with possibly hematuria added. However, in other insidious forms no clinical manifestation may be present, as exemplified by the reported case. Roentgen examination is indis-

pensable; the perirenal mass, and a partially or completely occluded kidney are seen on the pyelogram, with retrograde pyelography being normal. The loss of the psoas and kidney shadows as well as the displacement of the viscera indicates the extent of the lesion. Other signs which may point to this lesion are elevation of the diaphragm and antalgic scoliosis. Nephrotomography is of some value but a definitive diagnosis is obtained by renal angiography.

The differential diagnosis of perirenal hematoma secondary to infarct may, at times, prove quite difficult.

The following lesions should be considered: (a) perinephritic abscess; (b) renal neoplasm, which may be hard to eliminate. The age of the patient and the absence of cardiopathy are important factors; (c) rupture of a renal artery aneurysm may be demonstrated by angiography;20 (d) ruptured aortic aneurysm presents a dramatic clinical picture which includes profound shock; (e) adrenal hemorrhage may be suspected, especially in the newborn, after obstetrical manipulations; (f) neuroblastoma; (g) Wilms' tumor, if ruptured, is extremely difficult or even impossible to diagnose; (h) rupture of the kidney whether due to hydronephrosis, trauma or some idiopathic cause will be evident by extravasation of injected contrast medium, when given intravenously; (i) adrenal tumors, benign or malignant, usually do not affect renal function; and (j) perinephritis or paranephritic tumors may compress a renal pedicle and cause a renal infarct. 18,16

EVOLUTION

The evolution of the renal infarct with perirenal hematoma depends on the extent of the lesion. Death may occur or a healing process with scarring may take place. Infection of these hematomas is, nevertheless, dangerous. If the infarct is very extensive, aseptic autonephrectomy may occur. In a few months, the kidney will shrink to a hypoplastic size. In the interval, arterial hypertension may develop but it will usually be only temporary. In a smaller infarct,

the surface of the kidney retracts in 8 to 15 days and only a cortical incisure remains. Some perirenal hematomas may become cystic, calcified or ossified⁸ or may be completely resorbed.

SUMMARY

A case is reported of a patient who developed a silent partial renal infarct with a perirenal hematoma.

The angiographic studies and surgical findings are discussed.

Greater awareness from a clinical and roentgenologic point of view seems warranted.

The causes, diagnosis and differential diagnosis as well as the evolution of this lesion are discussed.

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INCREASED DOSAGE OF CONTRAST MEDIUM IN ROUTINE INTRAVENOUS UROGRAPHY*

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RECENT reports^{1,3,4} have indicated that larger than usual quantities of contrast medium are of value in excretory urography in certain patients. The drainage systems are reported to be shown with greater clarity and fewer repeat examinations, delayed studies, and retrograde studies are required. Friedenberg and Carlin² suggested that an increased amount of contrast agent be used routinely with the dosage determined by the patient's body surface area. Amar¹ recommended a double dose of contrast medium when there is impaired renal function, suspected or known ureteral or pelvic obstruction, edema or inadequate dehydration, hypertension due to suspected renal ischemia, obesity or large body size, and inadequate preparation. He also felt that it had merit in the study of certain bladder lesions, and as a substitute for retrograde urography in specific situations. Ross, Wilson, Robards, and Thompson³ reported that the use of large doses of opaque medium materially improves film quality in the face of moderate renal function depletion. Uebersax and LeRudulier4 compared different methods of excretory urography and obtained best results with a double dose of contrast medium. There has been no significant increase in the number or severity of reactions with the use of increased amounts of contrast material.1 This was true in over 1,500 high dosage excretory urographic examinations performed by Ross and associates.3

To explore the possible value of employing larger quantities of contrast medium in routine excretory urographic examinations, it was decided to compare the results obtained with 30 cc. and with 50 cc. of 50 per cent sodium diatrizoate.* One hundred consecutive patients were used in this

study. Fifty patients received 30 cc. of the medium while 50 alternate patients received 50 cc. of the medium. All roentgenograms were interpreted by 5 radiologists who did not know the amount of opaque medium administered in any case. Roentgenograms were judged as to the level of opacification of the pelvocalyceal system and the ureters, and rated as good, fair and poor. Good opacification permitted detailed study of the pelvocalyceal and ureteral anatomy. Fair opacification permitted adequate gross evaluation but precise, detailed delineation of the renal structures was not possible. Poor opacification was not sufficient for evaluation other than the determination of the presence or absence of obstruction and dilatation. Results of this study are presented in Table 1.

CONCLUSION

In this small series of cases, no advantage or additional information was obtained by the routine use of increased amounts of contrast medium as judged by opacification of the pelvocalyceal system or of the ureters. The literature indicates that increased dosage is of value when renal function is depressed or when other circumstances exist that decrease the likelihood of good visualization. Since it does not appear to be of value as a routine procedure and involves increased cost, the administration of a larger than usual quantity of contrast medium in intravenous urography should be limited to specific indications.

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 $T_{ABLE}\ I$ comparison of opacification of pelvocalyceal region and ureters using 30 cc. and 50 cc. of contrast medium

	30 cc. of Contrast Medium			50 cc. of Contrast Medium			
	Good	Fair	Poor	Good	Fair	Poor	
Opacification of Pelvocalyceal Region							
Radiologist #1	31	16	3	29	14	7	
Radiologist #2	21	21	8	20	20	IO	
Radiologist #3	28	18	4	26	17	7	
Radiologist #4	21	24	5 8	20	22	8	
Radiologist #5	27	15	8	25	18	7	
Total	128	94	28	120	91	— 39	
Average	25.6 (51.2%)	18.8 (37.6%)	5.6 (1.2%)	(48%)	18.2 (36.4%)	7.8 (15.6%)	
Opacification of Ureters							
Radiologist #1	21	17	12	25	13	12	
Radiologist #2	9	20	21	17	19	14	
Radiologist #3	27	17	6	27	17	6	
Radiologist #4	16	27	7	22	21	7	
Radiologist #5	24	16	10	21	21	8	
Total	97	97	<u></u> 56	112	91	— 4 7	
Average	19.4 (38.8%)	19.4 (38.8%)	11.2 (22.4%)	22.4 (44.8%)	18.2 (36.4%)	9·4 (18.8%)	

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STUDY OF 3 CONTRAST AGENTS IN 2,234 INTRAVENOUS PYELOGRAPHIES*

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HE study reported herein was undertaken in the Department of Radiology of the Washington County Hospital in an effort to determine which medium would produce adequate visualization of the urinary tract with the fewest toxic effects on the patient.

The results obtained with each of 3 commonly used contrast media in performing intravenous pyelographies on 2,234 cases were recorded and analyzed. The first 683 consecutive patients received 50 per cent diatrizoate sodium solution (hypaque 50 per cent) as the contrast agent; the next 921 consecutive patients received 60 per cent methylglucamine diatrizoate solution (renografin 60 per cent) and the final 630 consecutive patients received 66.8 per cent sodium iothalamate solution (conray-400).

Even though a dosage up to 30 cc. of contrast medium may be utilized in performing intravenous pyelography, in this study all adults received 20 cc. of the contrast medium instead of the higher dosage and instead of reduced dosages for quite ill or thin patients. None of the patients showed a significant reaction until after all of the medium had been injected. Children received 1 ml./kg. of body weight. There was no selectivity utilized to eliminate any specific type of disease. Both hospital patients and outpatients were examined as they were referred.

SOURCE OF DATA

A mimeographed form was utilized in collecting the data about each patient. The x-ray technician completed the part of the form concerning the patient's age, sex, provisional diagnosis (or chief complaint in the

absence of a provisional diagnosis), contrast medium used and reaction to the injection if any occurred. The completed form, the requisition slip and the resulting pyelograms were then examined by a radiologist who completed the form at the time of the interpretation of the roentgenograms by filling in the results as to "good," "fair" or "poor." The criteria for these groups were as follows: Excretion of a dense concentration of contrast medium with filling and visualization of all major and minor calyces, infundibula, pelves and almost all of each ureter placed the study in the "good" category; cases showing less concentration, even though there was incomplete visualization of all the portions of the components of the urinary tract but in which the radiologist felt that the study was diagnostically adequate were classified as "fair"; unsatisfactory visualization of the urinary tract or roentgenograms which could not be interpreted were placed in the "poor" group.

At the completion of data collection, the forms were coded for a National Cash Register 390 Computer and the resulting tabulations were submitted to statistical study.

The coding of the data was classified as follows:

- A. Age and Sex.
- B. Diagnosis:
 - 1. Urinary disease or symptoms.
 - 2. Diseases usually associated with urinary tract disease.
 - 3. Diseases not related to urinary disease. (In the accompanying tables, these are referred to as "urinary," "associated" and "unrelated.")
- C. Results: Good, fair or poor.

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 $T_{\rm ABLE}\ I$ number and per cent distribution of patients examined by age and sex according to medium used

	Both	Sexes	M	ales	Fen	nales	Per Cen
Medium and Age	No.	Per Cent	No.	Per Cent	No.	Per Cent	Males
All Media							
All Ages	2,234	100.0	1,163	100.0	1,071	100.0	52.1
0-19	281	12.6	114	9.8	167	15.6	40.6
20-49	927	41.5	428	36.8	499	46.6	46.2
50-69	703	31.5	380	32.7	323	30.2	54.1
70+	323	14.5	241	20.7	82	7.7	74.6
Hypaque							
All Ages	683	100.0	388	100.0	295	100.0	56.8
0-19	70	10.2	30	7.7	40	13.6	42.9
20-49	288	42.2	149	38.4	139	47 · I	51.7
50-69	216	31.7	124	32.0	92	31.2	57.4
70+	109	16.0	85	21.9	24	8.1	78.0
Renografin							
All Ages	921	100.0	463	0.001	458	100.0	50.3
0-19	124	13.5	45	9.7	79	17.2	36.3
20-49	385	41.8	160	34.6	225	49.1	41.6
50-69	288	31.3	165	35.6	123	26.9	57.3
70+	124	13.5	93	20.1	31	6.8	75.0
Conray-400	STATE OF THE PROPERTY OF THE P						
All Ages	630	100.0	312	100.0	318	100.0	49.5
0-19	87	13.8	39	12.5	48	15.1	44.8
20-49	254	40.3	119	38.1	135	42.5	46.9
50-69	199	31.6	91	29.2	108	34.0	45.7
70+	90	14.3	63	20.2	27	8.5	70.0

D. Side Effects: Nausea, vomiting, fainting, shock or severe reaction, hives, hiccups, pain in arm, sneezing, hot flushes, stuffiness of nose or ears.

RESULTANT DISTRIBUTION OF CASES AMONG THE THREE MEDIA

A. Age (Table 1). Very little difference existed in the age distribution. A slightly lower percentage of patients 0–19 years of age and a slightly higher percentage of patients 70 years and older were administered hypaque than were given the other 2 media.

B. Sex (Table 1 and 11). Of the patients in whom renografin and conray-400 were used, about 50 per cent were males, whereas 56.8 per cent of the hypaque patients were

males. This excess proportion of males in the hypaque group was largely among patients with urinary conditions.

C. Broad Disease Groups (Table 11). Most of the patients seen (1,549 or 69.3 per cent) had urinary diseases; 7.7 per cent were related conditions; and 23.0 per cent unassociated. Among the cases administered hypaque, a somewhat lower proportion (61.3 per cent) had urinary disease, and a higher proportion was unrelated to urinary conditions than was true of the other 2 media.

QUALITY OF PYELOGRAMS BY PATIENT CHARACTERISTICS (TABLE III)

A. Age. The quality of the pyelograms, varied in accordance with the age of pa-

tients, the youngest having the highest proportion of good results and the oldest having the highest proportion of poor results. This association between age and quality is statistically significant.

B. Sex. Males showed a lower proportion of good results and higher proportions of fair and poor results than females. This association is statistically significant. Part of the association between quality of pyelograms and sex is due to the higher proportion of males in the oldest age group (see Table 1), where results were poorest. In the vounger age groups, under the age of 50 years, there was relatively little difference between males and females in quality of pyelograms, but a substantial sex difference was noted among patients over 70 years of age. In patients 19 years of age and under, 97.6 per cent of the females showed good results compared to 92.1 per cent of the males. In the 20 to 49 year age group, 92.0 per cent of the females showed good results and 91.6 per cent of the males. In the 50 to 69 year old age group, good results were obtained in 82.0 per cent of the females and in 73.7 per cent of the males, while in those over 70 years of age, 73.2 per cent of the females had good results and only 52.7 per cent of the males.

C. Broad Disease Groups. The quality of the pyelograms was related to the broad disease groups into which the patients were classified, principally because of the low proportion (74.9 per cent) of good quality pyelograms among the "associated" conditions. Of the diseases classified as "associated," almost one-third (32 per cent) were heart ailments which were heavily concentrated in the older age groups, and in which cases only 67 per cent had good pyelograms. This accounts in large part for the lower proportion of good results among associated conditions as a whole.

Table II

NUMBER AND PER CENT DISTRIBUTION OF PATIENTS EXAMINED BY SEX AND DISEASE GROUP

ACCORDING TO MEDIUM USED

Medium and Disease	Botl	Sexes	M	ales	Fe	males	Per Cent
Group	No.	Per Cent	No.	Per Cent	No.	Per Cent	Males
All Media	egyang (Mahada Byagayang Africa) (gang alphabata) ng ganakada kata ganak			- Commence of the control of the con		and the second s	
All Groups	2,234	100.0	1,163	100.0	1,071	100.0	52.1
Urinary	I,549	69.3	859	73.9	690	64.4	55.5
Associated	171	7.7	82	7.1	89	8.3	48.0
Unrelated	514	23.0	222	19.1	292	27.3	43.2
Hypaque			THE PARTY OF THE P			An interest of the second	
All Groups	683	100.0	388	100.0	295	0.001	56.8
Urinary	419	61.3	262	67.5	157	53.2	62.5
Associated	65	9.5	33	8.5	32	10.8	50.8
Unrelated	199	29.1	93	24.0	106	35.9	46.7
Renografin			processing and processing and and finding				
All Groups	921	100.0	463	100.0	458	100.0	50.3
Urinary	685	74.4	364	78.6	321	70.1	53.1
Associated	6ī	6.6	34	7.3	27	5.9	55.7
Unrelated	175	19.0	65	14.0	110	24.0	37.1
Conray-400							
All Groups	630	100.0	312	100.0	318	100.0	49.5
Urinary	445	70.6	233	74.7	212	66.7	52.4
Associated	45	7.1	15	4.8	30	9.4	33.3
Unrelated	140	22.2	64	20.5	76	23.9	45.7

		PYELOGRAMS	BY PATI	ENT CHARACI	TERISTICS	3	_				
A. D. J.		Quality of Results									
Patient Characteristic		Ali	G	Food		Fair]	Poor			
	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent			
All Patients	2,234	1∞.0	1,851	82.9	257	11.5	126	5.6			
A. Age (yr.) 0-19 20-49 50-69 70+	281 927 703 323	100.0 100.0 100.0	268 851 545 187	95·4 91.8 77·5 57·9	9 62 111 75	3.2 6.7 15.8 23.2	4 14 47 61	1.4 1.5 6.7 18.9			
B. Sex Male Female	1,163	100.0 100.0	904 947	77·7 88.4	174 83	15.0	85 4 ^I	7·3 3.8			
C. Disease Groups Urinary Associated	1,549 171	100.0	1,284 128	82.9 74·9	176 32	11.4 18.7	89	5·7 6.4			

439

85.4

49

Table III

NUMBER OF PATIENTS EXAMINED AND PER CENT DISTRIBUTION OF QUALITY OF
PYELOGRAMS BY PATIENT CHARACTERISTICS

SIDE EFFECTS BY PATIENT CHARACTERISTICS (TABLE IV).

514

100.0

Unrelated

A. Age. The proportion of patients with one or more side effects was significantly associated with age. The highest proportion was 7.7 per cent in the age group 20 to 49 years, and the lowest proportion, 2.8 per cent in the oldest age group, 70 and older.

B. Sex. Although 5 per cent of the males and about 6 per cent of the females showed side effects, this difference is not statistically significant; that is, the difference could be due to chance in a sample of this number of cases.

C. Broad Disease Groups. About 3.5 per cent of the patients with conditions associated with urinary disease had side effects, 6.8 per cent of those with unrelated conditions, and 5.2 per cent of the urinary group. Although in larger samples these figures might be meaningful, in this sample of cases there is no statistically significant difference in the proportion of side effects among the several disease categories.

D. Relationship of Side Effects and Quality

of Pyelograms. As shown in Table IV, there is little difference in the percentage of side effects among patients in whom good or fair results were obtained, but about II per cent of those with poor results had one or more side effects.

9.5

26

5.I

Comment. Side effects were determined and recorded on the basis of observation by the radiologist or technician. Fainting, vomiting, severe reactions, sneezing, etc., were objective enough to be recorded in each case. However, when such effects were not obvious, the patient was asked if he felt all right. Sometimes, this question brought forth a description of certain subjective feelings such as stuffiness of the nose or ears or feelings of nausea. No specific symptom was suggested to the patient by the technician in the questioning. Only complaints as expressed by the patient were recorded. It cannot be stated that any particular group such as elderly or males complained more readily than any other group. It was unlikely, therefore, that any such subjectivity in response had any influence on the relationship between side effects and the type of contrast agent employed, as discussed in the following sections.

QUALITY OF PYELOGRAMS AND SIDE EFFECTS IN RELATION TO TYPE OF CONTRAST MEDIUM USED OVER-ALL RESULTS

It has been pointed out that the quality of the pyelograms and the side effects may vary in relation to age, sex, and possibly by general disease classification (Table III and IV). It has also been observed that the patient populations for which each of the 3 media were employed differed somewhat with respect to age, sex, and disease category (Table 1 and 11). It is difficult, therefore, to evaluate the relative efficacy of the 3 media unless each of the 3 is placed on the same standard with regard to patient characteristics; that is, to determine the numbers and proportions of quality of pyelograms and side effects that would occur for each median in a hypothetical population

TABLE V

QUALITY OF PYELOGRAMS AND SIDE EFFECTS EX-PECTED IN STANDARD POPULATIONS OF I,000 PA-TIENTS, ACCORDING TO TYPE OF MEDIUM

Medium	Qualit	y of Pyelo	ograms	With
Used	Good	Fair	Poor	Side Effects
	per	cent of ca	ses expec	ted
Hypaque Renografin Conray-400	78.2 82.7 88.3	13.4 12.3 8.1	8.4 5.0 3.6	7.2 4.1 5.4

that was identical for each median. In Tables v, vI, vII and vIII, the standard or hypothetical population used is I,000 patients having the same distribution of characteristics (age, sex or disease) as the total population of 2,234 patients included in the study. Table v shows the expected results when this procedure of standardization is carried out.

With respect to quality, the association of good, fair and poor results with the type

Table IV

NUMBER OF PATIENTS EXAMINED AND PER CENT WITH SIDE EFFECTS BY PATIENT CHARACTERISTICS

Patient Characteristic		All	With Si	de Effects	Without	Side Effects
Fatient Characteristic	No.	Per Cent	No.	Per Cent	No.	Per Cent
All Patients	2,234	100.0	121	5.4	2,113	94.6
A. Age (yr.)	**************************************					
0-19	281	1∞.0	12	4.3	269	95.7
20-49	927	1∞.0	71	7.7	856	92.3
50-69	703	1∞,0	29	4.1	674	95.9
70+	323	100.0	9	2.8	314	97.1
B. Sex						
Male	1,163	100.0	58	5.0	1,105	95.0
Female	1,071	100.0	63	5.9	1,008	941
C. Disease Groups						
Urinary	1,549	100.0	80	5.2	1,469	94.8
Associated	171	100.0	6	3.5	165	96.5
Unrelated	514	1∞.0	35	6.8	479	93.2
D. Quality of Pyelograms						,
Good	1,851	1∞.0	93	5.0	1,758	95.0
Fair	257	100.0	14	5.4	243	94.6
Poor	126	1∞.0	14	11.1	112	88.9

of medium used is statistically significant; that is, there are significant differences in results produced by the 3 media compared as a group and also when the media are compared 2 at a time, one against another.

The preferred order in quality is conray, renografin and then hypaque.

With respect to side effects, the association with the type of medium employed is also statistically significant. When taken in

Table VI $\\ \text{Quality of pyelograms and side effects expected in standard populations of 1,} \\ \text{ompatients by age according to type of medium used}$

Medium Used and	Standard	Qu	ality of Pyelogr	ams	With Side
Age of Patient	Population	Good	Fair	Poor	Effects
TT			(no. of cas	es expected¹)	
Hypaque All Ages	1,000	782	704	84	70
O-IQ	1,000	115	134 6	· .	72
- 1		378	26	5	7
20-49 50-69	415	11	64	24	40
70+	315	227 62	38	· 1	19 6
70-	144	02	30	44	0
Renografin					
All Ages	1,000	827	123	50	4I
0-19	126	122	3	I	3
20-49	415	374	35	6	27
50-69	315	240	51	24	9
70+	144	91	34	19	2
Conray-400					
All Ages	1,000	883	81	36	
O-I9	1,000	122	1	0	54
20-49		H	4 20	2	7 29
50-69	415	393 269	32		-
70+	315	11	25	14 20	13
/O-T	144	99		cases expected)	5
Hypaque			per cente or		1
All Ages	100.0	78.2	13.4	8.4	7.1
0-10	100.0	91.3	4.8	4.0	5.6
20-49	100.0	91.1	6.3	2.7	9.6
50-69	100.0	72.1	20.3	7.6	6.0
70+	100.0	43.1	26.4	30.5	4.2
, .					-
Renografin			Ī		
All Ages	0,001	82.7	12.3	5.0	4.I
0-19	100.0	96.8	2.4	0.8	2.4
20-49	1∞.0	90.1	8.4	1.4	6.5
50-69	100.0	76.2	16.2	7.6	2.9
70 +	100.0	63.2	23.6	13.2	I.4
Conray-400					
All Ages	100.0	88.3	8.1	3.6	5.4
0-19	100.0	96.8	3.2	0.0	5.6
20-49	100.0	94.7	4.8	0.4	7.0
50-69	100.0	85.4	10.2	4.4	4.I
70+	100.0	68.8	17.4	13.9	3.5

¹ Rounded to the nearest whole number.

Table VII $\\ \text{QUALITY OF PYELOGRAMS AND SIDE EFFECTS EXPECTED IN STANDARD POPULATIONS OF 1,} \\ \text{PATIENTS BY SEX ACCORDING TO TYPE OF MEDIUM USED}$

Medium Used and	Standard	Qu	ality of Pyelogr	ams	With Side
Sex of Patient	Population	Good	Fair	Poor	Effects
			(no. of cas	ses expected ¹)	<u> </u>
Hypaque					
Both Sexes	1,000	782	134	84	72
Male	521	376	87	58	32
Female	4 79	406	47	26	40
Renografin		America			
Both Sexes	1,∞∞	827	123	50	41
Male	521	407	84	30	23
Female	4 79	420	39	20	18
Conray-400					
Both Sexes	1,000	883	81	36	54
Male	521	438	56	27	22
Female	479	445	25	ģ	32
	415	113		cases expected)	ii 5
Hypaque				1	Automore
Both Sexes	100.0	78.2	13.4	8.4	7.2
Male	100.0	72.2	16.7	II.I	6.r
Female	1∞.0	84.8	9.8	5 - 4	8.4
Renografin					
Both Sexes	1∞.0	82.7	12.3	5.0	4.1
Male	1∞.0	78.i	16.1	5.8	4.4
Female	100.0	87.7	8.1	4.2	3.8
Conray-400					
Both Sexes	100.0	88.3	8.1	3.6	5.4
Male	100.0	84.1	10.7	5.2	4.2
Female	100.0	92.9	5.2	1.9	6.7

¹ Rounded to the negrest whole number.

pairs, the side effects with hypaque are significantly higher than those with renografin, but not significantly higher than the side effects with conray; nor are the side effects with conray significantly higher than those with renografin. Lack of statistical significance does not mean that there may not be a real difference; it means that the difference cannot be judged to be true, with 95 per cent confidence, from the results obtained in this particular study and sample size. One would judge from the above results that, with regard to side effects, renografin may be superior to hypaque and conray may be superior to

hypaque and inferior to renografin, but this cannot be stated with the same degree of confidence.

RESULTS BY AGE

The levels of the quality of pyelograms and side effects shown in Table v vary by patient characteristics within each of the several media used. Table vi indicates by age the number of patients with good, fair, or poor results, and the number with side effects that would be expected from intravenous pyelography in 1,000 patients with the same characteristics as those observed in this study. Also, in Table vi the percent-

Table VIII $\\ \text{QUALITY OF PYELOGRAMS AND SIDE EFFECTS EXPECTED IN STANDARD POPULATIONS OF 1,000} \\ \text{PATIENTS BY DIAGNOSTIC GROUP ACCORDING TO TYPE OF MEDIUM USED}$

Medium Used and	Standard	Qu	ality of Pyelogr	ams	With Side
Diagnostic Group	Population	Good	Fair	Poor	Effects
		- AUGUSTA	(no. of cas	ses expected1)	
Hypaque					[
All Groups	1,000	782	134	84	72
Urinary	693	532	96	65	47
Associated	77	58	17	2	4
Unrelated	230	192	21	17	21
Renografin					
All Groups	1,000	827	123	50	41
Urinary	693	579	83	31	28
Associated	77	54	15	8	I
Unrelated	230	194	25	11	12
Conray-4∞					
All Groups	1,000	883	81	36	54
Urinary	693	617	51	25	37
Associated	77	61	IO	6	4
Unrelated	230	205	20	5	13
Omulaced	2,50	203	1	cases expected)	
Hypaque			1	l	II
All Groups	100.0	78.2	13.4	8.4	7.2
Urinary	100.0	76.8	13.9	9.4	6.7
Associated	100.0	75.3	22.I	2.6	5.2
Unrelated	100.0	83.5	9.1	7.4	9.1
Renografin	i				
	100.0	90 =	100		
All Groups	100.0	82.7	12.3	5.0	4.1
Urinary	100.0	83.5	12.0	4.5	4.0
Associated	100.0	70.1	19.5	10.4	1.3
Unrelated	100.0	84.3	10.9	4.8	5.2
Conray-400					
All Groups	1∞.0	88.3	8.1	3.6	5.4
Urinary	100.0	89.0	7.4	3.6	5.3
Associated	100.0	79.2	13.0	7.8	5.2
Unrelated	100,0	89.1	8.7	2.2	5.6

¹ Rounded to the nearest whole number.

ages expected within each age group are shown. Here again, one sees that age for age conray-400 provided better results than either of the other 2 media. However, in the younger age groups, 0–19 and 20–49 years of age, hypaque provided good results in about 91 per cent of the cases as compared to 90–97 per cent for renografin or conray-400. The largest differences

in the results among the media existed with respect to older patients. Renografin produced fewer side effects than the other media within each age group. Within any one age group, the difference in the absolute number of patients who would be expected to have side effects is small, and it is a matter of judgement as to the medium to be employed in weighing the quality of re-

sults against the probability of producing the side effects.

RESULTS BY SEX

For each medium used, lower proportions of males than of females had good quality pyelograms (Table vII). Within each sex, the pyelograms were best with conray-400 and poorest with hypaque. Among males, renografin produced only a slightly higher proportion (5.8 per cent) of poor pyelograms than did conray-400 (5.2 per cent), but renografin showed a higher proportion of pyelograms which were only fair (16.1 per cent). Among both males and females, there were more side effects with hypaque than with either of the other media. Among females, use of renografin resulted in a lower percentage of side effects than did conray-400, but among males, there was substantially no difference in the side effects from these two contrast agents.

RESULTS BY BROAD DISEASE GROUPS

The general pattern of results by the broad disease groupings used was consistent in that, within each medium used, conditions unrelated to urinary disease had, by a small margin, the largest proportion of cases with good quality pyelograms, followed closely by the cases with urinary conditions (Table VIII). Good results were achieved least frequently in cases associated with urinary disease. Again, in general, conray-400 showed the best results and hypaque the poorest. An apparent deviation from this generality existed for the category of conditions "associated" with urinary disease. In this study, hypaque showed a higher proportion of good pyelograms (75.3 per cent) than did renografin (70.1 per cent). This difference is not statistically significant and may be due to chance. It would be of interest to determine by further study whether there are true differences in results achieved with hypaque and renografin by type of disease.

SUMMARY

The results of a study of 2,234 unselected patients undergoing intravenous pyelographies, employing 3 commonly used contrast agents are reported.

Observations were recorded as to the quality of the pyelograms obtained and the side effects noted in the patients. The data were analyzed with respect to age, sex and general disease group for the study population as a whole, and with respect to the types of contrast agents employed.

The choice of contrast agent should ideally be individualized according to the age, sex and disease group of the patient in order to obtain a high probability of complete visualization of the urinary tract with low probability of adverse side effects. Such a procedure would be indicated if there were gross divergencies of results from the contrast agents among different age-sex-disease categories of patients, or it might be indicated for a radiographic office or department which has high proportions of children or of elderly patients. However, in the usual busy general hospital radiology department, it is impractical to stock several agents and tailor their use to an advance assessment of individual patient characteristics. The choice is to be made, therefore, on the basis of the agent which gives the best concentration and the fewest side effects in the greatest number of patients regardless of age, sex, or disease category. The authors feel that their preference of the contrast media for intravenous pyelography would be: first, renografin; second, conray-400; and third, hypaque. The data presented in this report may provide some guides for selection of a contrast agent in relation to the type of radiology department or office in which it is to be used.

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THE NORMAL PYELOGRAM UREA WASHOUT TEST*

A STUDY OF 33 NORMOTENSIVE CONTROLS

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HE pyelogram urea washout test, introduced by Amplatz in 1962, is a popular and valuable test for the identification of patients whose hypertension may be based on a correctable renovascular lesion.2,4,5,6,7 Few false positives have been reported, and false negative studies must be extremely uncommon. Patients with renal artery stenosis and a positive washout test on the same side are good candidates for corrective or reconstructive surgery, and the cure or improvement rate is high in such patients.5,7

The pyelogram urea washout test is based upon the following physiologic considerations. An underperfused kidney responsible for systemic hypertension reabsorbs water and sodium at a more rapid rate than the opposite uninvolved kidney. Since the commonly employed aqueous iodinated roentgenographic contrast agents are filtered by the glomeruli and not reabsorbed by the tubules, reabsorption of water at a rapid rate on the affected side results in hyperconcentration of the opaque material in the kidney collecting system on that side. This difference in the concentration of the opaque material is usually not discernible in the dehydrated state. It can, however, be consistently demonstrated by induction of a marked osmotic diuresis using urea; the underperfused side retains the contrast substance and remains visible while the normal side becomes diluted and washed out. Thus, the disparity in the roentgenographic appearance of the two sides will become obvious, and the characteristic physiologic abnormality associ-

ated with renovascular hypertension may be visually perceived. A unilaterally positive test is represented by rapid washout of the opaque material in the normal kidney collecting system with retention of the opaque material in dense concentration in the abnormal kidney.

The conventional renal split function study or Howard test depends upon comparison of urinary abnormalities on the suspected abnormal side with the opposite side for a control. Consequently, bilateral disease will likely go undetected by this test. It was originally hoped that the pyelogram urea washout test might afford a convenient and reliable means of predicting bilateral renovascular disease; a bilaterally positive washout test would be expected to show retention of the opaque material on both sides in fairly dense concentration for perhaps 12 to 18 minutes following the start of the urea infusion. Several hypertensive patients with this finding have been encountered, and bilateral disease was suspected. It was supposed that a bilaterally positive test would indicate bilateral renal underperfusion.

Previous conclusions regarding the roentgenographic appearances which may be considered to represent positive and negative washout tests have largely been drawn from experience with hypertensive patients upon whom the test was performed for diagnostic purposes. In order to help establish the response of normal kidneys in nonhypertensive patients to the pyelogram urea washout test and thereby provide a normal standard, 33 normal human volun-

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teers were examined. This communication is a report of the results of the washout test in this control group.

SELECTION OF SUBJECTS

Thirty-three healthy, young volunteers ranging in age from 21 through 29 years (average age 25 years) were examined. Each had multiple blood pressure determinations, and the average ambulatory blood pressure in all subjects was less than 120 /80. Each had a negative urine analysis; the urine was tested for specific gravity, protein and sugar and was examined microscopically by one of us (G.H.S.). There were 31 Caucasians and 2 Negroes (both males), 31 males and 2 females. None of the volunteers had a history of renal or other chronic disease.

METHOD OF STUDY

Each of the examinations was performed early in the afternoon. There was no routine premedication, and preparation consisted of a laxative the night before, a light breakfast the morning of the examination, omission of the noon meal the day of the examination, and fluids as desired until noon the day of the examination, after which time nothing was taken by mouth until the examination was concluded.

Following the exposure of a preliminary film and after a negative intravenous test dose, 50 cc. of 75 per cent sodium and meglumine diatrizoate (hypaque-M, Winthrop Laboratories) was injected rapidly intravenously followed by filming at 30 seconds and 1, 2, 3, and 8 minutes. The films were developed promptly, and when a satisfactory pyelogram appeared on both sides, usually on the 8 minute film, the urea infusion was begun (ordinarily 15-20 minutes after the contrast injection). This infusion was prepared by dissolving 40 gm. of urea (ureaphil, Abbott Laboratories) in 500 cc. of normal saline. This was infused over a 15 minute period at a constant rate, during and following which time films were exposed at the rate of I every 3 minutes. The examination was ordinarily completed with

the film exposed 21 minutes after the start of the urea infusion, though on occasion roentgenograms were made for a slightly longer time. As soon as the urea infusion was completed, 500 cc. of normal saline was administered over a 15 to 20 minute period and additional fluid was given by mouth. At the end of this period, the patient was transferred to a recovery area within the department, where he remained supine for an additional 60 minutes and was encouraged to take oral fluids. At the end of that period, he was dismissed.

In 1962, Marshall and Hinman⁸ reported a death in a 54 year old male from a subdural hematoma following urea administration during a split renal function study (Stamey test). These authors speculated that the hypertonic urea produced cerebral dehydration with subsequent retraction of the brain surface from the dura and tearing of the bridging veins. They advocated prompt restoration of normal tonicity of the body spaces and maintenance of the horizontal position for 12 hours in order to decrease the hazards of producing a subdural hematoma under these circumstances. In order to determine the magnitude of the dehydration produced by the pyelogram urea washout test and in order to determine the efficacy of our efforts at rehydration, blood samples were drawn in 12 of the control subjects immediately prior to beginning the urea infusion, immediately after the urea infusion was complete, and about 20 minutes later at the end of the rehydration period in the roentgenographic room and before the patient was transferred to the recovery area for further administration of fluids by mouth. Using the Fisk Osmometer, serum osmolarity was determined on these 3 blood samples in each of 12 control subjects and in 13 hypertensive subjects in whom the test was performed for diagnostic purposes.

RESULTS

On the early films a nephrogram effect was produced, and renal length could be measured. The average length of the right





Fig. 1. Normal control. Usual appearance of negative washout test. (A) Baseline pyelogram shows opacification of both kidney collecting systems. (B) Film exposed 18 minutes after the start of the urea infusion shows dilution of the contrast material and complete washout of the pyelogram on each side.

kidney was 13.3 cm. and the average length of the left kidney was 13.5 cm. in this series. Renal size on the right ranged from 11.9 cm. to 15.5 cm.; on the left the range was from 11.9 cm. to 15.9 cm. In only 2 patients was there a disparity in renal length of greater than 1 cm. on the two sides. In 1 of these patients, the right kidney was 12.3 cm. long and the left was 13.5 cm. long. In the other, the right kidney was 13.6 cm. long and the left was 15.3 cm. long.

In all but I case, a pyelogram appeared simultaneously on the two sides. The earliest appearance time of the contrast material was 30 seconds and the latest appearance of the contrast material on the two sides was 3 minutes. In I subject, the pyelogram appeared within 2 minutes on the right side but was delayed until 3 minutes on the left. The pyelogram and wash-

out test were normal in this subject in every other respect. The average appearance time of the contrast material was the same on both sides and was between 1 and 2 minutes.

In most of the subjects, washout of the contrast material on the two sides began promptly after initiation of the urea infusion (average 7 minutes), and dilution and disappearance of the pyelogram on each side were complete in most patients a few minutes later (average 15 minutes) (Fig. 1, A and B). In a sizable number, however, washout of the contrast material from the collecting systems was not complete during the time of filming. In 8 of the 33 patients, contrast material could still be easily seen in both collecting systems when the examination was concluded. This was at least 21 minutes from the start of the urea infusion

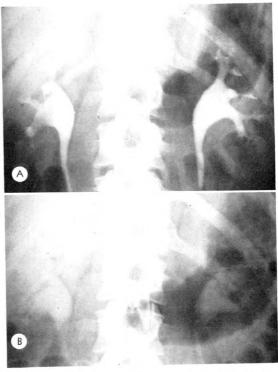


Fig. 2. Normal control. Bilateral retention of the contrast material. (A) Baseline pyelogram shows dense and equal opacification of both kidney collecting systems. (B) Film exposed 18 minutes following the start of the urea infusion shows faint but definite visualization of both kidney collecting systems. The density is the same bilaterally.





Fig. 3. Normal control. Bilateral retention of the contrast material. (A) Baseline pyelogram shows dense and equal concentration of the contrast substance. (B) A film exposed 30 minutes following the start of the urea infusion shows fair opacification of both collecting systems. Some dilution has occurred, but both are still clearly and equally visible.

and in most patients was from 30 to 35 minutes. Examples of bilaterally delayed washout are illustrated in Figures 2 through 5.

In 2 patients, a disparity in the time of washout on one side compared with the other side was noted (Fig. 6, A, B and C; and 7, A, B and C). This appearance simulated a unilaterally positive test. In both cases, however, the appearance was not persistent, and both collecting systems were subsequently diluted and washed out within a normal period of time. The disparity in apparent rate of washout on the two sides was probably due to contraction of the renal pelvis on the side with the apparently rapid washout. The disparity did not persist.

The average serum osmolarity prior to the infusion of urea was 286 mosm./kg. H_2O (range 274 to 301) in the control sub-

jects. This average figure rose to 320 immediately following the infusion of 40 gm. of urea in 500 cc. of normal saline (range 286 to 344) and returned to an average value of 296 following modest efforts at rehydration (range 276 to 315). Comparable average figures in the 13 hypertensive subjects were as follows: prior to urea, 283 mosm./kg. H₂O; immediately after urea, 319; following rehydration, 297. It may thus be seen that while the urea infusion produced an elevation in serum osmolarity, it had returned to normal (295 mosm./kg. H₂O) by the time the patient left the

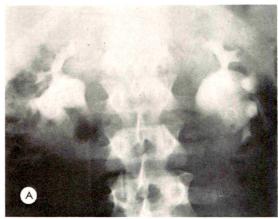




Fig. 4. Normal control. Bilateral retention of the contrast material. (A) Baseline pyelogram shows dense opacification of both kidney collecting systems. An extrarenal pelvis is present on each side, the left being considerably larger than the right. (B) A film exposed 21 minutes following the start of the urea infusion shows dense concentration of the contrast agent on both sides despite the osmotic diuresis induced by urea. Little if any washout has occurred.

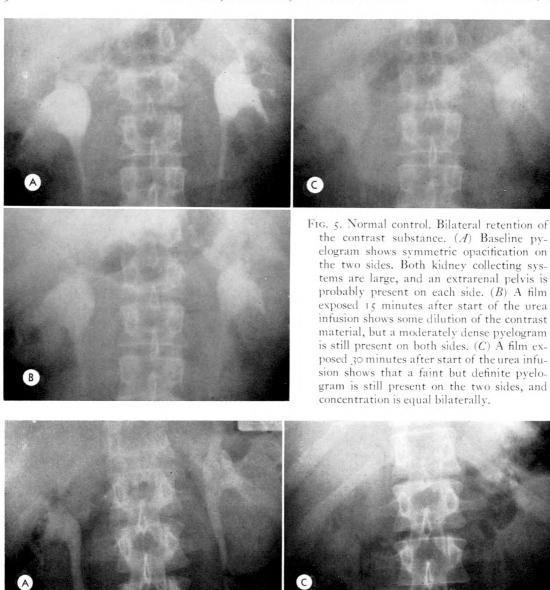
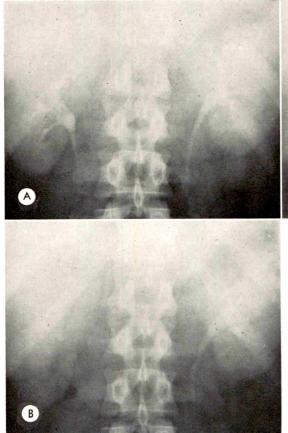


FIG. 6. Normal control. A unilaterally positive test is simulated. (A) Baseline pyelogram shows bilaterally equal opacification of the collecting systems. (B) A film exposed 3 minutes following the start of the urea infusion shows absence of a pyelogram on the right with dense concentration of the contrast agent on the left. This appearance simulates a positive test on the left but is presumably due to contraction and emptying of the collecting structures on the right.

(C) A film exposed 12 minutes following the start of the urea infusion shows bilateral washout of the contrast agent. The test is negative in this control subject since both sides wash out equally in 15 to 18 minutes.



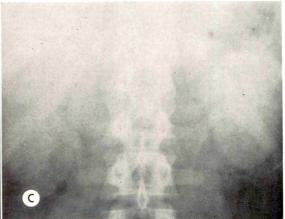


Fig. 7. Normal control. A unilaterally positive washout test on the left is simulated. (A) Baseline pyelogram shows bilaterally equal opacification of the kidney collecting structures. (B) A film exposed 12 minutes following the start of the urea infusion shows complete washout of the collecting system on the right, with faint but definite retention of the contrast agent on the left. (C) A film exposed 18 minutes after start of the urea infusion shows bilaterally symmetric washout of the contrast agent. The apparent unilateral retention on the left in B was presumably due to peristaltic contraction of the kidney collecting system on the right.

roentgenographic room following intravenous administration of 500 cc. of normal saline and several cups of water by mouth.

DISCUSSION

The interesting variety of unusual findings uncovered in the study of 33 healthy normotensive volunteers and described and illustrated above must be considered to fall within the range of normal in interpretation of the pyelogram urea washout test.

In the great majority of normal subjects studied, renal length was less than I cm. different on the two sides. In the average case, a pyelogram appeared simultaneously on the two sides in less than 2 minutes. Following the start of the urea infusion, dilution and washout of the contrast-filled collecting structures began between 6 and 9 minutes later and was complete between 15 and 18 minutes from the start of the

urea infusion. In most of the examples reported here, there was no evidence of selective unilateral retention of the opaque material or of bilateral visualization of the collecting structures past 18 minutes.

However, in 2 subjects, there was more than I cm. discrepancy in renal length, and in I normal subject initial visualization of the renal collecting structures was delayed for about I minute on the left side by comparison with the right. In 2 subjects, a falsely positive test was suggested on one side by rapid disappearance of the pyelogram unilaterally while the opposite side became diluted and washed out in the expected time. That was probably due to contraction of the renal pelvis and ureter on the involved side, and the apparent disparity in time of disappearance of the pyelogram did not persist on subsequent films, both sides becoming washed out within the expected period of time. Stejskal *et al.*⁷ have enumerated and illustrated many of the causes of a falsely positive washout test, including unilateral larger collecting system, overlying intestinal contents, unilateral renal pelvic contraction, anomalies of rotation, obstruction and unilateral renal parenchymal disease.

One of the most interesting findings encountered in this study was the rather high incidence of bilateral retention of the contrast material in a concentration sufficient to allow visualization even on the films exposed as late as 27 to 35 minutes following the start of the urea infusion. In some, the concentration was sufficient to have suggested the possibility of bilateral renovascular lesions had the patients been hypertensive, and in I patient (Fig. 4, A and B), the concentration of the opaque material was as dense 21 minutes after the start of the urea infusion as it was prior to the start of the infusion. In that patient, there was a large extrarenal pelvis on the left and the ureter took origin from that pelvis at a curious angle. It may be argued that an anomaly of rotation was present on that side, and the possibility of some degree of mild and perhaps clinically inconsequential ureteropelvic junction obstruction may also be postulated as a cause of contrast material retention. However, on the right side, which was morphologically normal, the same degree of retention of the opaque material was seen, and there was no roentgenographic evidence of obstruction or anomalous position on that side. The patient was normotensive and in good health. Hence, judging from this case and some of the others with bilateral opacification of the contrast-filled collecting structures on films exposed after the conclusion of the urea infusion, we may tentatively conclude that it will likely be impossible to utilize the pyelogram urea washout test for the detection of bilateral renovascular lesions.

The data concerning alterations in serum osmolarity due to the hypertonicity of the serum produced by the urea diuresis and the restoration of normal tonicity following infusion of 500 cc. of normal saline and about 500 cc. of water by mouth suggest that fears regarding the possible consequences of the rapid cerebral dehydration produced by osmotic diuresis during the test are unfounded. If rehydration is produced by the suggested method and if the patient is kept in the recumbent position for about an hour following the conclusion of the examination, no ill effect should be anticipated.

SUMMARY AND CONCLUSIONS

The results of the pyelogram urea washout test in 33 normotensive healthy young volunteers are reported. On the average, no disparity in renal length greater than I cm. or delay in appearance time was found, and the presence of a pyelogram on both sides was visible within 2 minutes of the end of the injection of the contrast material. Washout of the pyelogram commenced between 6 and 9 minutes following the start of the urea infusion and was complete between 15 and 18 minutes. A difference in the response of the collecting systems on the two sides was not ordinarily noted, and bilateral retention of the contrast substance was generally not seen. There were, however, exceptions to these findings in several of the control examinations, and the following conclusions, some of which have been previously reported, seem war-

- I. Disparity in renal length of more than I cm. may be a normal finding in some persons.
- 2. Slight difference in appearance time of the contrast material on the two sides may rarely be found in a normal subject (1 out of 33 in this series).
- 3. A falsely positive test may be simulated by unilateral contraction of the collecting structures (2 of 33 in this series). In both of these cases, however, both collecting systems were equally diluted and washed out in the expected period of time, and the apparent unilateral retention of the opaque material was a finding that did not persist on the later films.

- 4. A "bilaterally positive" pyelogram urea washout test is probably valueless in the detection of bilateral renovascular disease responsible for hypertension since retention of the contrast material on both sides following urea diuresis was observed in 8 of 33 controls. Its most important use continues to be as a screening test, since false negatives are exceedingly uncommon.
- 5. Serum osmolarity studies indicate that return of normal tonicity of the body fluids can be expected following the dehydration produced by urea diuresis provided that certain simple efforts at parenteral and oral rehydration are effected.

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DRIP INFUSION PYELOGRAPHY*

ITS EVALUATION AS A ROUTINE EXAMINATION

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THE introduction of drip infusion pyelography had stirred the hope that the perfect antegrade method of studying the urinary tract had been developed. Examinations that were initially unsatisfactory and had been salvaged by large dose pyelography are familiar to those using this technique.^{3,5,6,7} If this procedure were used routinely and more satisfactory studies result, then the increased cost would be justified. The following investigation was instituted in an attempt to find an answer to this question.

MATERIAL

Patients referred to the radiology department for urinary tract examinations at the Columbia Presbyterian Medical Center were divided into 4 groups; those injected with a diatrizoate compound* in doses of: (1) 25 or 50 cc., the latter being used for all patients over 30 years of age or over 150 pounds in weight; (2) 1 cc. per pound; (3) and (4) I cc. per pound and an equal quantity of 5 per cent dextrose and water. Groups 1, 2, and 3 were dehydrated; hydration represented the only difference in the protocol between Groups 3 and 4. A minimum dose of 150 cc. of contrast material as stipulated by Schencker⁵ was used in Groups 2, 3 and 4. Dehydration consisted of no fluids or food by mouth from 12 midnight to the time of the examination and varied from 9 hours to 18 hours. Catharsis was not routinely used. The ages of the patients ranged from the second to the eighth decade and there was an equal division between the sexes. Only patients showing marked impairment of excretion or an obstructive uropathy were

excluded from a series. The study was considered satisfactory if there was good delineation of the pelvocalyceal structures, the ureters, and the presence of a nephrogram (Fig. 1).

ROENTGEN TECHNIQUE OF THE EXAMINATION

Group 1: 25 or 50 cc. of contrast material. The first film was exposed 5 minutes after the injection of contrast material. The compression device was then applied and after 5 minutes of compression, roentgenograms in anterior and oblique projections of the abdomen were obtained. The block was then released and a 15 minute roentgenogram was obtained. Pre and post voiding cystograms were then made. Subsequent views, if indicated, were also obtained. The ureteric compression device was an inflatable dual balloon device which permitted roentgenography in oblique projections with ureteric compression.



Fig. 1. Excellent detail and contrast are present. Ureteric compression was used and the injected dose was 25 cc. of renografin 60.

^{*} In the form of renografin 60.

^{*} From the Department of Radiology, Columbia-Presbyterian Medical Center, College of Physicians & Surgeons, New York, New York.

Table I

RESULTS OF VARIOUS INJECTIONS

(renografin 60)

			(3)	(4)
In per cent	(1) 25 or 50 cc.	(2) 1 cc./pound	1 cc./pound+5% c	lextrose and water
			Dehydrated	Hydrated
Satisfactory	95%	82%	89%	90%
Nephrogram	72%	99%	95%	99%
Ureter Seen	76%	87%	88%	97%
Nephrogram Interferes	0	42%	47%	32%
Diuresis	4%	36%	45%	41%
No. of Cases	93	55	81	101

Groups 2, 3 and 4: 5 minutes after the start of the infusion, a film in anterior projection of the abdomen was exposed. Anterior and oblique projection roentgenograms of the abdomen were obtained between 20 and 30 minutes. Subsequent roentgenograms were similar to those of Group 1. The time required for the infusion averaged 5 minutes using an 18 gauge needle. No ureteric compression was employed. The illustrations of drip infusion pyelograms used in this article are all from Group 4. Similar findings were encountered in Groups 2 and 3.

RESULTS AND DISCUSSION

The material was divided into satisfactory and unsatisfactory pyelograms and the adequacy of each type of examination is shown in Table I. No effort was made to subdivide the satisfactory studies into excellent or average examinations since this was not felt to be important. The percentage of satisfactory studies was highest in the group injected with 25 or 50 cc. of contrast material (Table II). However, all groups yielded a high percentage of satisfactory pyelograms.

All radiologists and urologists are familiar with the usual causes of poor diagnostic studies: inadequate filling of the collecting system (Fig. 2, A and B). This was also found in high dose pyelography (Fig. 3, A

and B), but, in addition, other significant limitations were encountered. The most prevalent was the appearance of a nephrogram so dense that the pelvocalyceal system, delineated by low density contrast material, was obscured (Fig. 4, A and B). Early opacification of the collecting system in rapid sequence pyelography was difficult to identify, especially if bowel gas was present and this seriously limited the value of this study. Thus, the high dose of contrast material in routine pyelography offers a distinct disadvantage. This technique is excellent for nephrotomography since 99 per cent of the patients will demonstrate a dense tubular nephrogram. Whether this study will produce the same diagnostic accuracy as the capillary-tubular nephrogram of Evans et al.2 is yet to be deter-

Table II

COMPARISON OF INFUSION STUDY TO 25 OR 50 CC. DOSE INTRAVENOUS INJECTION (renografin 60)

The	25 or 50 cc.	dose was:	
	Better	Same	Worse
Group 2	IO	2	3
Group 3	8	6	3
Group 4	5	IO	I

The majority of comparison studies were in cases of gross urinary tract disease and are excluded.





Fig. 2. (A) The initial study with 50 cc. of renografin 60 was unsatisfactory. (B) After infusion of 150 cc. renografin 60 with an equal quantity of 5 per cent dextrose and water, an excellent diagnostic study was obtained.

mined. It is our impression that similar information is available in both forms of nephrotomography.

The profound diuresis that is produced by the hypertonic contrast material and intravenous fluid causes the excretion of very low concentrations of contrast material into the pelvocalyceal structures and overdistention of the collecting system in a significant number of examinations. There is, undoubtedly, an optimum quantity of intravenously injected contrast material that will densely opacify the collecting system, but with an increase beyond this quantity there will be a diuresis and, therefore, lower density contrast material in the collecting system (Fig. 5, A and B). This was well demonstrated in the present study,

both with the routine dose and large dose pyelography. The patients exhibiting these findings are not felt to have intrinsic renal disease and the diuresis may well be secondary to body water reserves and an inability of the tubules to concentrate urine when presented with a high water load.

The appearance of an overdistended urinary tract can be a source of error in patients with a partial obstruction at the ureterovesical junction (Fig. 6, A and B). Delayed roentgenograms will show persistence of contrast material with an obstruction and will exclude the possibility of error, but unfortunately, if the suspicion is not aroused on the initial roentgenograms of the abdomen, delayed studies will not be obtained. To eliminate this error an early film at 5 minutes is included in the filming series. But, frequently, diuresis is already



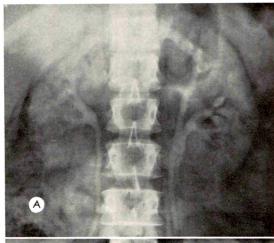


Fig. 3. (d) The initial study with 50 cc. renografin 60 was unsatisfactory as is the infusion study (B). Although slight improvement is present, retrograde pyelography is necessary.

seen at 5 minutes, and the possibility of error is not eliminated.

The entire course of the ureters is most frequently seen in the infusion type examination, especially on one single roentgenogram (Fig. 7). However, a high percentage of cases, after the injection of 25 or 50 cc. of contrast material, had the ureters entirely delineated. It was necessary to have several projections in this examination, each demonstrating a portion of the ureter.

The dilated appearance of the pelvocalyceal system and ureters in a group raised the question of its cause. It has been proposed that a decreased transport of urine across the ureterovesical junction was a source of the dilated ureters and pelvis.⁴



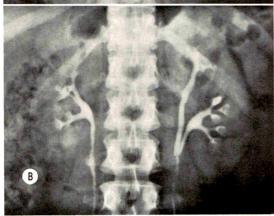
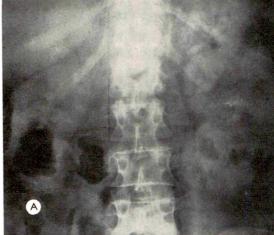


Fig. 4. (A) The infusion pyelogram is a poor study in comparison to (B) the earlier examination performed with 25 cc. renografin 60.



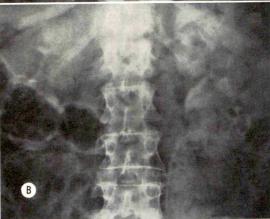


Fig. 5. After infusion, roentgenograms at (A) 3 and (B) 30 minutes were obtained. Although a diuresis appearance is not present (Fig. 4A), the density is equally low and the study is unsatisfactory.

The individuals showing this effect were usually men having symptoms of prostatism. This appearance was infrequently seen in younger age groups, although in all age groups excellent visualization of the pelvocalyceal system and ureters without dilatation could be found.

The main purpose of the infusion study proposed by earlier authors^{3,5,6,7} is the salvage of the examination with a poorly visualized urinary tract. The result here is 50 per cent, a very rewarding percentage of patients that will not need retrograde pyelography.

Many patients with elevated blood urea nitrogen levels, in excess of 100 mg. per

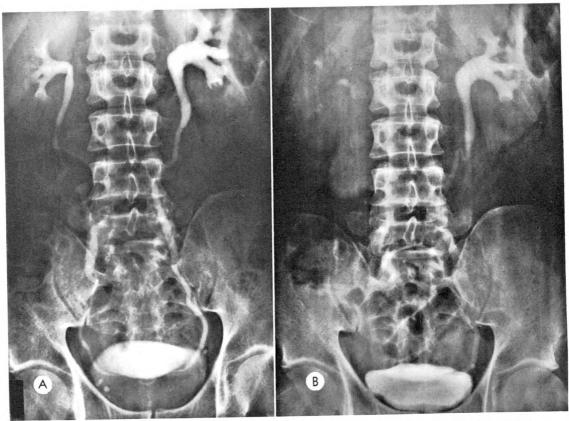


Fig. 6. A nonopaque stone was present at the left ureterovesical junction. (A) There is slightly greater dilatation on the left with (B) confirmation of the obstruction in the 2 hour study.



cent, can frequently have diagnostic studies with infusion pyelography.

SUMMARY

Infusion pyelography is not indicated as the routine intravenous examination. There is no greater incidence of satisfactory diagnostic studies than with lower dose methods. Artefacts of technique, profound nephrogram and diuresis are distinct disadvantages.

The value of this form of urography for the examination of the patient with impaired renal function and for nephrotomography is confirmed.

The method is indicated after an unsat-

Fig. 7. Excellent delineation of pelvocalyceal system, ureters and bladder.

isfactory urographic study and prior to retrograde pyelography.

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THE EFFECT OF DRIP INFUSION PYELOGRAPHY ON RENAL FUNCTION*

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THE administration of large volumes of contrast medium markedly increases the diagnostic capabilities of intravenous urography. Of the various techniques, we have found drip infusion pyelography^{4,5,7,8,11} to be the best. It is easy to perform and gives consistently excellent nephrograms and visualization of the upper and lower urinary tracts.

Reported toxicity of drip infusion pyelography has not been greater than that of conventional low dosage intravenous urography. However, review of the literature has failed to reveal information concerning specific effects of drip infusion pyelography on renal function. We decided to investigate this effect.

METHOD AND MATERIALS

In 10 randomly selected patients, ranging in age from 18 to 62 years, renal function was evaluated by determination of urine volume, glomerular filtration rate, renal plasma flow, and osmolar clearance during 2 consecutive 15 minute collections immediately before and after infusion for drip infusion pyelographies. Because good urine volumes for reliable clearance studies were needed, the patients were well hydrated. Blood urea nitrogen was determined before and 24 hours after infusion pyelography. Blood pressure and pulse rate were measured throughout the study on each patient.

The infusion was composed of I cc. of 50 per cent sodium diatrizoate (hypaque*) mixed with I cc. of 5 per cent dextrose in water per pound of body weight and was given through a 19 gauge needle in an ante-

cubital vein. The infusion bottle was elevated above the patient the length of the infusion set tubing and allowed to flow unrestricted. Administration took 5 to 10 minutes.

Glomerular filtration rate was measured by the clearance of endogenous creatinine as described by Homer Smith⁹ and renal plasma flow was measured by the clearance of radio hippuran (I¹³¹) as described by B. G. Smith and associates.¹⁰ Urine was collected by indwelling bladder catheter.

RESULTS

Following drip infusion pyelography, a marked increase in osmolar clearance in all patients and in urine volume in all but I patient occurred. The changes in renal plasma flow and glomerular filtration rate were not as consistent. Three patients had marked decreases in renal plasma flow and 4 patients had marked decreases in glomerular filtration rate. One patient had an appreciable increase in glomerular filtration rate. Changes of less than 10 per cent are within the range of normal variation in our laboratory (Table 1). A signed rank test,⁸ used to test the significance of the differences between the values before and after drip infusion pyelography, indicated that the observed differences in osmolar clearance and urine volume are statistically significant, P=.001, while those in renal plasma flow and glomerular filtration rate are not.

No patient had a significant change in blood urea nitrogen, blood pressure or pulse rate during his study. Despite the state of hydration, good urograms were obtained.

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[†] Research Trainee under U. S. Public Health Service Grant CRT-5057.

	Renal Plasma Flow (per cent)	Glomerular Filtration Rate (per cent)	Urine Volume (per cent)	Osmolar Clearance (per cent)
I	-9.3	-38.9	+52.0	+129.4
2	-6.5	-26.1	+79.6	+139.0
3	+2.5	-8.6	+14.7	+304.1
4	-22.3	-12.5	+8.9	+22.6
5	+5.4	-6.9	-21.4	+21.2
6	-2.0	-0.5	+162.1	+128.7
7	+9.8	+24.5	+138.5	+82.1
8	-6.8	+0.∞1	+76.8	+48.0
9	-11.5	-17.5	+16.3	+33.4
CI	-16.8	-2.6	+24.4	+100.4

Table I

PER CENT OF CHANGES FOLLOWING DRIP INFUSION PYELOGRAPHY

DISCUSSION

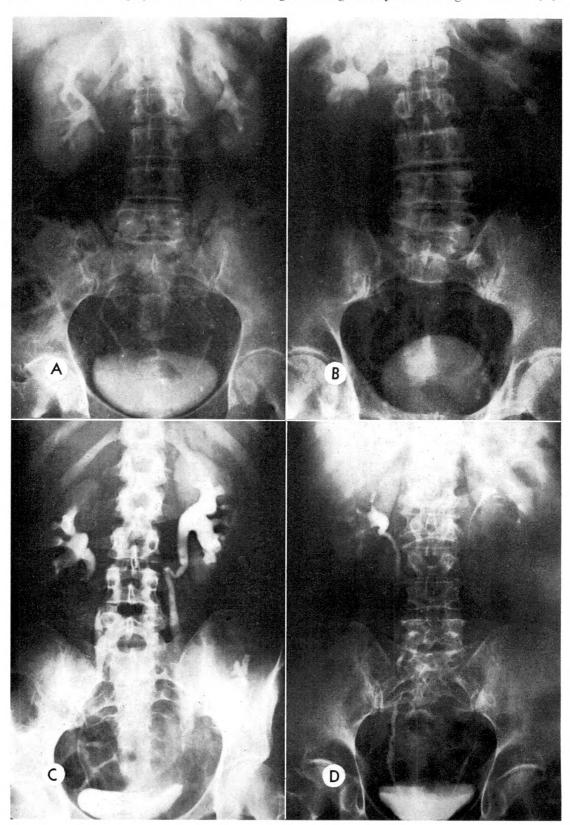
Drip infusion pyelography gives such excellent urograms, even in hydrated patients, that we now use it almost routinely rather than the standard low dosage intravenous pyelography, except in patients with cardiac decompensation. (For patients with diabetes mellitus, normal saline solution instead of dextrose in water is mixed with the contrast medium to make the infusion solution.) Drip infusion pyelograms usually eliminate the need for retrograde contrast studies, and even in markedly uremic patients good urograms are frequently obtained.

In the 256 drip infusion pyelographies we have performed to date, there have been no major reactions. The incidence of minor reactions (urticaria, nausea, vomiting, rhinitis, sneezing, headache) has been 8 per cent, which is approximately the incidence we have observed with standard intravenous pyelography. These findings are similar to those of other investigators of drip infusion pyelography.4,5,7,8,11 Accurate data for further comparison are difficult to obtain, for if the reaction is not a significant systemic one, detection is difficult and frequently missed. The over-all true incidence of standard low dosage intravenous pyelography reactions is not known.

The etiology of contrast medium toxic reactions has not been proven. The most

popular theories are that the reaction is anaphylactoid with small arteries the main antibody-antigen reaction site and that certain individuals have a quantitative idiosyncrasy and react qualitatively at a lower dose in the same manner that everyone would respond to if given enough. Harris and Harris⁴ report that patients who experienced mild transient allergic reactions after administration of 25 cc. of 50 per cent hypaque did not react during or after drip infusion pyelography.

Diminishing the rate of contrast medium administration has not resulted in greater safety. Rapid injection of large volumes of highly concentrated newer tri-iodinated contrast media has been found to be well tolerated.2 Our data would seem to substantiate this finding. There was no significant change in renal plasma flow, glomerular filtration rate, blood pressure, pulse rate, or blood urea nitrogen following drip infusion pyelography. However, the data suggest a trend towards a decrease in renal plasma flow and glomerular filtration rate (Table 1). It is possible that with larger dosages of contrast medium, this trend would become significant. The most marked effect of the rapidly given infusion of contrast medium was the significant increase in urine volume and osmolar clearance. These changes are the result of the renal handling of hypaque which, like inulin, is



filtered by the glomeruli with no tubular reabsorption or secretion. The presence of hypaque in the tubules osmotically obligates water, thus increasing urine volume. Diuresis floods the urinary system with highly concentrated contrast medium, producing consistently excellent opacity of calvees, pelves, and ureters (Fig. 1, A-D), and satisfactory cystograms and voiding urethrograms. Since the nephrogram is a result of vascular, glomerular, and tubular factors, loading renal tubules and collecting ducts with contrast medium probably is also a factor in the very dense nephrograms obtained. Ureteral opacity is so good in most patients that retrograde studies usually are not needed.

SUMMARY

Drip infusion pyelography consistently results in dense nephrograms and excellent opacity of the upper and lower urinary tracts. This is secondary to flooding the urinary system with highly concentrated contrast medium.

The effect of drip infusion pyelography on glomerular filtration rate, renal plasma flow, urine volume, osmolar clearance, blood pressure, pulse rate, and blood urea nitrogen was studied. The only significant effect was a marked increase in urine volume and osmolar clearance. Drip infusion pyelography has no deleterious effect upon kidney function and presents no greater incidence of toxic reactions than the low dosage standard intravenous pyelography. This method greatly increases the capabilities of intravenous urography, frequently eliminating the need for retrograde contrast studies.

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Fig. 1. Drip infusion pyelograms. (A) Normal 5 minute postinjection roentgenogram demonstrating the dense nephrogram and opacity of the renal pelves, ureters and bladder. Roentgenograms are routinely taken at 1, 5, 10 and 20 minutes after infusion. (B) Good visualization in 5 minutes despite chronic renal disease secondary to benign prostatic hypertrophy. At the time of this study, patient's blood urea nitrogen was 46 mg. per cent. Standard intravenous pyelogram showed "inadequate visualization." (C) Excellent opacity of the upper tract and ureters showing distal left ureteral fistula following ureterolithotomy. (D) Left renal cyst. These characteristically appear as sharply circumscribed, rounded radiolucencies.

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THE CHANGES ON THE INTRAVENOUS PYELOGRAM IN RENAL ARTERY DISEASE*

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IN THE last few years there has been an increasing interest in renal artery disease as a cause of hypertension, largely because the development of renal arteriography has shown that this type of lesion is appreciably more frequent than previously thought. Renal arteriography is not entirely free from morbidity and even mortality, however, and although some centers perform routine arteriographies on all moderate or severe hypertensive patients, most centers would seem to prefer some form of screening test.

The most frequent and the simplest diagnostic screening test is the intravenous pyelogram, and the intention of the author is to review a consecutive and unselected series of 68 pyelograms in hypertensive patients on whom renal arteriographies were performed. The great majority of patients were investigated entirely at the Ottawa General Hospital, but a certain number, who were referred from other hospitals for renal arteriography, had intravenous pyelograms available only from the referring source.

The series consisted of 39 males and 29 females, ranging in age from 16 to 70 years. The purpose of the review is to determine the accuracy with which the various pyelographic criteria were found to predict the presence of renal artery disease, unilateral or bilateral.

ROENTGENOGRAPHIC CRITERIA OF RENAL ARTERY DISEASE

I. ASYMMETRY OF LENGTH WITHOUT PARENCHYMATOUS THINNING

The occurrence of asymmetry of the kidneys in unilateral renal artery disease was first noted by Poutasse and Dustan¹⁷ in 1956 and by Hodson¹⁰ independently in

1957. Poutasse and Dustan¹⁸ in 1957 suggested that 1.0 cm. or more was a significant degree of asymmetry, and this criterion has been widely quoted and accepted. Hodson considered that asymmetry of 1.5 cm. or more was significant, particularly if accompanied by "generalized narrowing of the renal substance on the smaller side," and this figure for asymmetry of length is also quoted, but little attention has been paid to the question of accompanying thinning of the renal substance even though Poutasse¹⁶ in 1961 stated that an important sign is "a difference in the length of the kidneys of I cm. as measured on the roentgenogram, with a corresponding decrease in the thickness of the renal cortex, indicating some form of atrophy of the smaller kidney, possibly due to a deficient arterial blood supply.'

In assessing the significance of renal asymmetry, it must be borne in mind that the kidneys are normally asymmetric, the right kidney tending to be shorter than the left; this is a fact well known anatomically, and it has been shown roentgenographically.6,7,8,11,14 More important for this purpose than the average difference in length are the accepted limits of normal variation. The present author analyzed a series of 100 normal intravenous pyelograms in adults with normal blood pressure; "normal" intravenous pyelograms excluded both pathologic lesions and anatomic variations such as duplex kidney. Asymmetry of 1 cm. or more was found in 27; asymmetry of 1.5 cm. or more was found in 9 of these 27 (Table 1). In addition to length, what was termed "parenchymatous thickness" was also assessed; this was the distance between the tips of the renal papillae and the lateral aspect of the kidney outline at the

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 $T_{\rm ABLE} \; I$ asymmetry in normal kidneys (1 ∞ cases)*

I. Asymmetry of length

Asymmetry less than 1.0 cm. 73

Asymmetry 1.0 cm.-2.4 cm. 27 over 1.5 cm. in 9/27

shorter kidney was on the right in 25/27

II. Asymmetry of parenchyma

Asymmetry less than 1.0 cm. 73 Asymmetry 1.0 cm. or over 27

parenchymatous asymmetry variable shorter kidney thicker in 20/27 shorter kidney same in 5/27 shorter kidney thinner (I mm.) in 2/27

mid-level of the lateral aspect of the kidney. It should be noted that this measurement is inaccurately termed "cortical thickness" by some authors; the measurement actually includes both cortex and medulla. From this consideration, and from a small series of proven cases of renal artery disease, the conclusion was drawn that asymmetry of length of 1 cm. or more is probably significant only when accompanied by parenchymatous thinning of the affected kidney.

In the present series of 68 cases, asymmetry of 1 cm. or more, unaccompanied by parenchymatous thinning, was encountered in 7 cases (Table II); in 3, the asymmetry was over 1.5 cm.

The renal arteriograms revealed renal artery lesions in only 1, a patient with asymmetry of 1.4 cm. In the remaining 6

patients, the renal arteriograms were normal; representative cases are illustrated in Figures 1, A and B; and 2, A and B. The absence of a renal artery lesion in 6 of these 7 cases would suggest that asymmetry of length alone is not significant.

2. ASYMMETRY OF LENGTH WITH PARENCHYMATOUS THINNING

Asymmetry of 1.0 cm. or more was accepted as significant if accompanied by parenchymatous thinning of 3.0 mm. or more compared with the opposite side.⁶ Renal function was assessed by comparison of the concentration and apparent volume of opaque medium on the 2 sides. Comparison of concentration was relatively simple to perform, but comparison of volume was less easy and apparent diminution of volume was only accepted if it was a constant

TABLE II
INCIDENCE OF INTRAVENOUS PYELOGRAPHIC CHANGES IN RENAL ARTERY DISEASE

	Total	Renal Artery Lesion	No Renal Artery Lesion
No. of Cases	68	29	39
Asymmetry without Parenchymatous Thinning	7	I	6
Asymmetry with Parenchymatous Thinning +impaired function	17	17	0
impaired function	6	= =	0
Impaired Function Alone	9	4	5
Hyperconcentration	0	0	0

^{*} Data reproduced by permission of the Editor of the Journal of the Canadian Association of Radiologists.

finding on all films of the examination, which at this hospital consists of 4 films exposed up to 21 minutes after injection.

(a) With normal function on intravenous pyelogram. Six patients had asymmetry of length with parenchymatous thinning, but without obvious impairment of renal function (Table II). Of these, all had unilateral renal artery lesions on aortography; Figure 3, A and B illustrates one such case.

(b) With impaired function on intravenous pyelogram. Eleven patients showed asymmetry of length with parenchymatous thinning together with apparent impairment of renal function on the affected side. In all these patients, the asymmetry was in fact more than 1.5 cm., and the parenchymatous thinning was marked. Impairment of function was revealed by both diminution of concentration of opaque medium and apparently diminution of volume. All 11 patients had renal artery lesions (Table 11), unilateral in 8 and bilateral in 3.

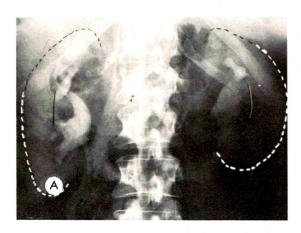




Fig. 1. (A) Right kidney 1.5 cm. shorter than left, parenchyma of equal thickness. (B) Renal arteriogram, normal.

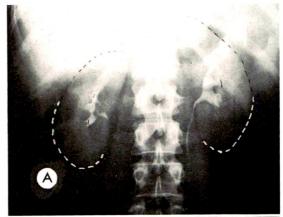


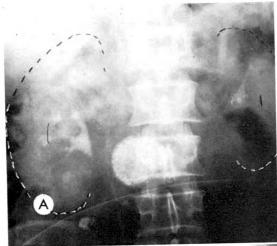


Fig. 2. (A) Right kidney 2.0 cm. shorter than left, parenchyma 0.6 cm. thicker. (B) Renal arteriogram, normal.

There was thus a total of 17 patients with asymmetry of the kidneys of 1.0 cm. or more (in 15, the asymmetry was in fact 1.5 cm. or more), accompanied by parenchymatous thinning. All 17, whether or not there was accompanying impairment of function on the intravenous pyelogram, had renal artery lesions, unilateral or bilateral.

3. DEPRESSED FUNCTION WITHOUT RENAL ASYMMETRY

If renal artery disease can produce renal shrinkage with or without obvious impaired function, it would seem possible that it can produce impaired function without renal shrinkage, and, in fact, most authors give impairment of renal function as a finding suspicious of a renal artery lesion, apparently independent of asymmetry of size.



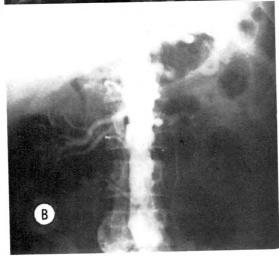


Fig. 3. (A) Left kidney 3.2 cm. shorter than right, parenchyma 2.1 cm. thinner. (B) Aortogram showing severe atheroma of abdominal aorta, with almost complete occlusion of the left renal artery.

In the present series, 8 patients were considered to have unilateral diminution of concentration and volume of opaque medium without significant asymmetry of renal size and I was considered to show diminished concentration on one side without diminution of volume. Of these 9 (Table II), 4 had renal artery lesions on the affected side (2 being bilateral) and I had a renal artery lesion on the opposite side. For reasons to be discussed later, this last case was considered to show impairment of concentration of opaque medium on one side rather than hyperconcentration on the other, and

was considered a false positive result. The 4 remaining cases showed no renal artery lesion. Figures 4, A and B; and 5, A and B illustrate the conflicting findings that may occur with apparent impairment of function.

It thus seems that evidence of unilateral impairment of function on the intravenous pyelogram, unaccompanied by asymmetry of size, is suspicious of a renal artery lesion and an indication for renal arteriography. It seems, however, much less reliable an indication than asymmetry of length with parenchymatous thinning, whether or not this is accompanied by impairment of function.



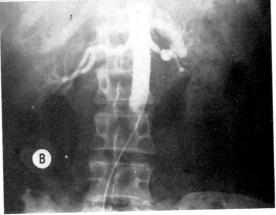


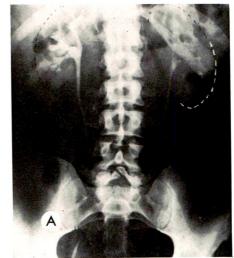
Fig. 4. (A) Kidneys symmetric in length. Apparent diminution of volume and concentration from left kidney, present on all four films of the pyelography. (B) Aortogram showing severe stenosis with poststenotic dilatation of the left renal artery and irregularity of right renal artery, suggesting fibromuscular hyperplasia.

4. INCREASED CONCENTRATION OF OPAQUE MEDIUM

Although it seems obvious that a kidney with impaired blood supply should produce a diminished concentration of opaque medium, reports appeared in 1959 of isolated cases of increased concentration from the affected kidney.4,15,19 This occurrence has been amply confirmed^{8,13,20,22} and seems to be quite frequent (30 per cent of 80 cases in the series of Scott and his colleagues²⁰). The mechanism appears to be2,4 a diminished glomerular filtration of opaque medium, with a slow passage through the tubules and hence increased tubular reabsorption of water. This is indeed the basis of the "washout" test^{1,2} for renal artery stenosis, whereby an artificial diuresis washes out the opaque medium from the normal, but not from the abnormal, kidney.

A surprising finding in the present series (Table II) was that no evidence of apparent hyperconcentration of opaque medium was detected either in those with or in those without renal artery lesions. One case was mentioned above, which was interpreted as showing diminished concentration of opaque medium on the left side and in which a renal artery lesion was discovered on the opposite side, and it might seem that this was in fact an instance of hyperconcentration from the affected kidney. Hvperconcentration of opaque medium, however, is associated with a diminution of volume of excretion from the affected side; as explained, this diminution of volume appears to be part of the mechanism of the hyperconcentration. In this case, the volume appeared diminished on the side with the poorer concentration, and it appears more probable that this was an instance of misleading concentration estimation.

There are two possible factors in the absence of evidence of hyperconcentration in this series. Peart¹⁵ has suggested that hyperconcentration will not occur if severe structural damage has occurred in the kidney, and this may account for its absence in some cases. The other factor to be considered is the presence of dehydration before intravenous pyelography. Hyperconcen-



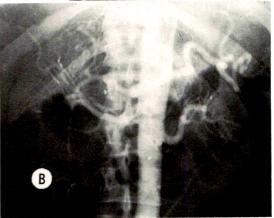
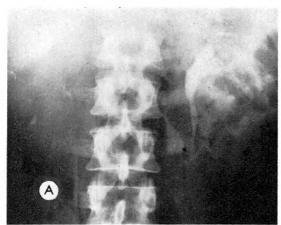


Fig. 5. (A) Right kidney 0.3 cm. shorter than left, no parenchymatous thinning. Apparent diminution of concentration and volume of opaque medium from the left kidney, present on all 4 films of the pyelography. (B) Renal arteriogram, normal.

tration on the affected side is best seen if there is good diuresis which will produce better dilution of the opaque medium on the normal side. All patients who had intravenous pyelographies at this hospital had total fluid restriction for at least 14 hours before the examination and this may have concealed the hyperconcentration on the affected side by producing a high concentration on the normal side.

5. DELAY IN APPEARANCE OF OPAQUE MEDIUM

Poutasse and Dustan¹⁸ in 1957 stated that "slight delay in appearance of radiopaque medium on one side may be indic-



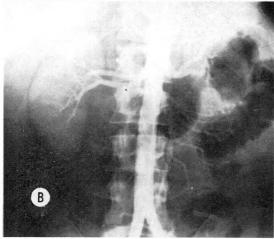


Fig. 6. (A) Four minute film shows apparent delay in appearance of opaque medium from the right kidney, which was no longer present by the 12 minute film. (B) Normal renal arteriogram.

ative of renal artery occlusive disease," and it is a common finding in the presence of obvious impaired function. However, Scott and Quesada²¹ found delay in the 5 minute film "so infrequent as to be of limited practical significance."

Maxwell and his associates^{3,12,13} noted that this delay is best seen in the roentgenograms taken within a few minutes of the injection, and made this the basis of rapid sequence intravenous pyelography, in which films are exposed at 1, 2, 3, 4, and 5 minutes after rapid injection of the opaque medium. Deyton and his colleagues⁵ reported on their results with a similar technique and stated that "differences in filling are most apparent in the 3 and 4 minute

radiographs and this appears to be the critical period of the procedure."

In this series, no rapid sequence pyelograms were obtained. The routine intravenous pyelographies, however, included a 4 minute film. In only one instance was apparent delay found without other evidence of abnormality; the renal arteriogram was normal (Fig. 6, \mathcal{A} and \mathcal{B}). In those with other evidence of renal artery disease, unilateral delay was found commonly.

In this series, therefore, the 4 minute study was only positive when there was other evidence of renal artery disease and did not contribute to diagnostic accuracy; it was, however, of value as a confirmatory procedure.

6. URETERIC NOTCHING

"Notching" or "scalloping" of the upper ureter has been reported as a sign of renal artery obstruction apparently from collateral arterial circulation to the affected kidney. 9,23 No instances of this sign were found in the present series even though 3 of the cases showed profuse collateral circulation around an obstructed renal artery on arteriography.

CONCLUSIONS AND SUMMARY

A series of 68 renal arteriograms for hypertension is reviewed with reference to the roentgenologic indications of renal artery disease on the intravenous pyelogram. Of the 68 cases, 29 had renal artery lesions, 21 unilateral and 8 bilateral. Of the 21 unilateral lesions, 19 occurred in the main renal artery and 2 in a major branch.

Asymmetry of length alone without parenchymatous thinning was not found to have any significant association with renal artery disease and is considered a normal anatomic variant.

Asymmetry of length of 1.0 cm. or more with parenchymatous thinning, whether or not accompanied by evidence of diminished function on the affected side, was found to be very good evidence of a renal artery lesion, unilateral or bilateral, and a strong indication for renal arteriography.

Impaired function (diminished volume and concentration) on the intravenous pyelogram without significant anatomic asymmetry of the kidneys was found to be a less reliable indication of renal artery lesion, but was, nevertheless, an indication for renal arteriography.

Despite the frequency of its occurrence in some reported series, hyperconcentration of opaque medium in an affected kidney was not found in this series.

Although delay on the 4 minute intravenous pyelogram was seen not infrequently in unilateral and bilateral renal artery lesions, it was present only when accompanied by other evidence of renal artery disease and did not contribute greatly to the accuracy of diagnosis from intravenous pyelography. No rapid sequence intravenous pyelographies, however, were performed.

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EXCRETORY UROGRAPHY IN RENOVASCULAR HYPERTENSION*

MINUTE SEQUENCE FILMING AND OSMOTIC DIURESIS

By DAVID M. WITTEN, M.D., JAMES C. HUNT, M.D., SHELDON G. SHEPS, M.D., LAURENCE F. GREENE, M.D., and DAVID C. UTZ, M.D.

THE detection of hypertension of renovascular origin is of recognized clinical importance, but its differentiation from hypertension of primary etiology is often exceedingly difficult. No one screening procedure has proven to be uniformly satisfactory; however, recent studies indicate that renal vascular lesions responsible for sustained diastolic hypertension may be suspected in many cases from alterations in renal mass and excretory function as demonstrated by excretory urography.1,3,4 Standard urographic techniques permit only qualitative estimation of renal function, yet differences in certain parameters of function of the separate kidneys may be detected from differences in the appearance times, the degrees of concentration, and the rates of excretion of contrast medium. The frequency of demonstration of these alterations in renal function may be increased by employing two techniques designed to more accurately record and augment these differences: (1) "minute" sequence filming which employs multiple film exposures early in the excretory urographic sequence to demonstrate minimal but significant differences in the times of appearance of medium in the two kidneys when functionally significant renal artery stenosis is present and (2) "washout" tests which employ osmotic diuretics, such as urea or mannitol, in combination with excretory urography to demonstrate graphically the hyperconcentration and the resulting delay in washout of medium associated with functionally significant renal lesions, parenchymal or vascular.

Correlation of the data obtained by these special urographic techniques with other parameters of renal function and with the various types of renal artery defects responsible for hypertension has not been well documented. The present study was undertaken in an effort to define further the place of minute sequence filming and of diuresis with a nonreabsorbable osmotic diuretic (mannitol washout test) in the urographic detection of hypertension of renovascular origin.

CASE MATERIAL AND METHODS

Thirty-two hypertensive patients undergoing extensive diagnostic evaluation because of suspected functionally significant, renovascular lesions were studied. All underwent conventional excretory urography and renal arteriography. Thirty-one of the patients had isotope renography by the standard technique employed at our institution.6 Sixteen had separated renal function studies, in which catheterization of both ureters was employed for the determination of renal hemodynamics and the handling of solute and water by the individual kidneys.2 Sixteen patients, including some but not all of 16 just mentioned, had hypertension and renal artery stenosis which was thought to be functionally significant and potentially surgically correctable. These patients underwent surgical exploration and vascular repair or nephrectomv.

For the purpose of this study, each of the 32 patients was also subjected to excretory urography employing minute sequence

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filming followed by osmotic diuresis with a nonreabsorbable solute as described in the following paragraphs.

Roentgenographic Technique: Minute Sequence Films and Mannitol Washout Test. The patient was prepared for examination by thorough laxative purgation the night before and by refraining from food and drink for at least 14 hours before the examination. No abdominal compression was used in the filming sequence. Preliminary roentgenograms were made while the patient was in the supine position. Twentyfive milliliters of sodium and methyl glucamine diatrizoates in a 69 per cent solution (renovist) were injected as rapidly as possible (within 3 to 5 seconds) through a 17 gauge needle inserted percutaneously into an antecubital vein. Films were exposed 30 seconds and 1, 2, 3, 4, and 5 minutes after injection. After the 5 minute film was exposed, a rapid infusion of 5 per cent mannitol (osmitrol) in 5 per cent dextrose in water was started. Within approximately 5 minutes, 300 ml. of the solution (15 gm. of mannitol) was infused. Films were exposed every 5 minutes starting from the beginning of infusion and continuing for 30 minutes. At the end of the examination, a standing roentgenogram was made to demonstrate renal ptosis. Approximately 45 minutes was required to complete each examination. The procedure was well tolerated by all patients and no untoward side effects were encountered.

Each examination was reviewed independently by I radiologist and 2 urologists who had no knowledge of the patient's clinical condition or of laboratory findings in the case. Data tabulated from the urographic studies included longitudinal length of the kidneys, time of appearance of medium, calyceal irregularities ("spidering"), and differences in the degree of concentration of medium. Rapid sequence films were recorded as positive if the medium appeared in the calyceal system of one kidney before it appeared in that of the other and negative if the medium appeared simultaneously in both kidneys. The man-

nitol washout test was recorded as positive if a clear-cut difference in washout of medium developed between the two kidneys during the period of observation and negative if the washout was equal for the two kidneys.

RESULTS

On the basis of arteriographic findings, the results of renal function studies, and other laboratory data, 16 patients were considered to have primary (essential) hypertension and 16 to have renal artery stenosis causative of hypertension. The results of the urographic and separated renal function studies are summarized in Table 1 for those patients having primary hypertension. Each of the 16 patients with primary hypertension had normal conventional excretory urograms; however, a disparity in renal size of greater than 1.5 cm. was present in 4 cases. Isotope renography revealed evidence of renal functional impairment consistent with renal or renovascular lesions in 13 of the 15 patients with primary hypertension who were studied by this technique. Aortography revealed normal renal arteries in II of these cases, unilateral renal artery stenosis of mild to moderate degree (less than 50 per cent stenosis) in 4, and unilateral incomplete renal artery occlusion resulting from subintimal placement of the catheter in 1. Separated renal function studies which were accomplished after arteriography gave abnormal results in the last mentioned case; however, studies in 3 of the 4 cases showing mild or moderate stenosing lesions revealed no evidence of a functionally significant lesion. One patient with mild stenosis has biochemical evidence suggesting possible primary aldosteronism, but this diagnosis has not as yet been proven. The minute sequence urogram was normal in all 16 cases of primary hypertension (except for the size differences noted on conventional urography). The mannitol washout test was positive for 2 of the 16 patients, and these patients also had arteriographic evidence of mild or mod-

Table I

PRIMARY HYPERTENSION: CORRELATION OF UROGRAPHIC AND SEPARATED RENAL FUNCTION STUDIES

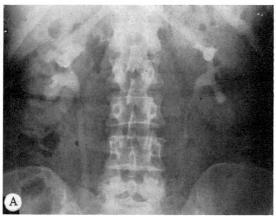
Renal Artery Stenosis	Case	Minute Sequence Urograms	Mannitol Washout	Separated Renal Function Studies
None	I to II	All negative	All negative	
Unilateral, mild to moderate	12	_	_	
	13	_	_	_
	14	_	+*	_
	15	-	+†	_
Unilateral, temporary‡	16	_	_	+

* Positive mannitol washout on side opposite mild renal artery stenosis.

† Positive mannitol washout on same side as mild renal artery stenosis.

‡ Right renal artery temporarily occluded by subintimal injection of medium.

erate unilateral renal artery stenosis; however, separated renal function studies revealed the lesions not to be functionally significant by our current criteria. The false-positive washout tests were on the same side as the lesion in I case and on the





opposite side in the other (Fig. 1, A and B).

Of the 16 patients having hypertension of renovascular origin (Table 11), 7 showed features suggesting possibly abnormal function by conventional urography. In 5 of the 7 cases, times of appearance of the medium were delayed. Three of these 5 patients had increased concentrations of medium on the involved side. The sixth patient had increased concentration of the medium alone, and the seventh had socalled spastic calvees on the involved side without other evidence of abnormality. Eleven of the 16 had a disparity in renal size to the extent that the pole-to-pole diameter of the involved kidney was smaller than that of the uninvolved by 1.5 cm. or more.

Minute sequence urograms showed delayed appearance times on the involved or more severely involved side in 9 cases; appearance times were normal in 7 cases. Isotope renography indicated either uni-

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Fig. 1. Case 14. Primary hypertension—false-positive result of mannitol washout test. (A) Five minute film exposed just before start of mannitol infusion. (B) False-positive washout is evident on right 15 minutes after start of mannitol infusion.

REMOVASCULAR HIPERIENSION; CORRELATION OF UROGRAPHIC AND FUNCTIONAL STUDIES				
Renal Artery Stenosis	Case	Minute Urogram Mannitol Washou		Separated Renal Function Studies
Bilateral L>R R>L L>R L>R L>R	17 18 19 20	- +, L +, L	- +, R +, L +, L	+, L>R +, R +, L>R +, L>R
Unilateral	21		_	+
Main renal artery	22 23 24 25 26 27 28 29 30 31	 - + + + + + +	- + + - + + + +	+ + + + + + +
Unilateral aberrant artery	32		+*	Unsatisfactory

Table II
RENOVASCULAR HYPERTENSION: CORRELATION OF UROGRAPHIC AND FUNCTIONAL STUDIES

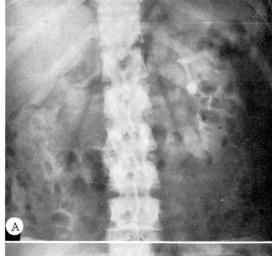
lateral or bilateral renal functional abnormalities consistent with renal vascular or parenchymal disease in each case. Aortograms revealed bilateral renal artery stenosis in 4 cases and unilateral stenosis in 12. (In 11 cases, the main renal artery showed stenosis and in 1, an aberrant artery.)

In the 4 cases of bilateral renal artery stenosis, separated renal function studies gave evidence of a functionally significant lesion on the side of the more severe stenosis and the data were indicative of bilateral renal vascular disease in 3 of the 4 cases. Minute sequence films showed disparity in appearance time in 2 of the 4 cases. Results of mannitol washout tests were positive for the side having functionally significant stenosis in 3 cases but were normal (as was the minute sequence test) in 1 case of severe bilateral stenosis.

Seven of the II patients thought to have functionally significant unilateral renal artery stenosis had separated renal function studies, all of which gave confirmatory (positive) results. Results of both the

minute sequence urograms and the mannitol washout were negative in 2 cases. Functional significance of the stenosis was demonstrated by separated renal function studies in both of these cases. In 2 other cases, the minute sequence test gave positive results, but the mannitol washout was negative. In 1 of these, a positive result was obtained with the separated renal function study on the side of the positive washout (Fig. 2, A, B and C). Function studies were not done in the other case. In 5 cases, both the minute sequence and the mannitol washout tests gave positive results on the side of the renal artery stenosis (Fig. 3, A, B and C). The separated renal function studies gave correspondingly positive results in 3 cases and were not done in the other 2. In the 2 remaining cases of unilateral functionally significant renal artery stenosis, minute sequence tests gave negative results, but results of the mannitol washout tests were positive. In one of these, the separated renal function study showed abnormal function corresponding to the

^{*} False-positive result of mannitol washout test on side opposite renal artery lesion.







positive mannitol washout (Fig. 4, A, B and C); in the second, this test was not done.

The single patient having functionally significant unilateral aberrant artery stenosis had negative results to the minute

Fig. 2. Case 25. Renovascular hypertension—severe stenosis of right main renal artery. (A) Positive result on right on minute sequence urogram. (B) Five minute urogram made just before start of mannitol infusion. (C) False-negative result of mannitol washout test.

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sequence test; however, the mannitol washout test gave false-positive results on the side opposite the renal artery lesion. The failure of the medium to wash out from the normal kidney in this case was apparently due to a minor anomaly of the renal pelvis which inhibited drainage of the kidney. Separated renal function studies were carried out in this case, but the study was considered not to be technically satisfactory because the urologist was able to catheterize only one ureter.

COMMENT

Minute sequence urography has been shown by Maxwell and his associates,3 as well as by others, to be a useful and practical adjunct to other clinical and laboratory data for evaluation of patients under study for hypertension of suspected renovascular origin. Unfortunately, this simple test has not proved to be sufficiently sensitive to detect functionally significant renal artery lesions in up to one-third of such cases. Unilateral increased concentration of medium, "spidery" or "spastic" calyces, retention of medium, disparity of renal size, and other urographically detectable abnormalities associated with functionally significant renal artery stenosis are of assistance in diagnosis in some cases but are, by and large, difficult to assess because of their nonspecific nature and have proved to be of limited value in diagnosis.

Amplatz¹ proposed the pyelogram-urea washout test as a sensitive urographic indicator of functionally significant renovascular disease, and subsequently Staab and his associates⁵ pointed out that this test can be used successfully for detection of these lesions when minute sequence urography is normal. Schreiber and his as-

sociates⁴ likewise studied the urea washout test. They used a modification of the Amplatz technique in 50 cases of hypertension and concluded that this test "... may be considered to be a reliable radiographic split renal-function test' when negative. When positive, the test is strongly suggestive of unilateral renal artery disease as the cause of hypertension."

The use of urea as a diuretic agent in the urea washout test has been the subject of some concern. Administration of urea in high concentration produces severe headaches in many cases, and there is thought to be at least some potential hazard from both intracerebral hemorrhage and "rebound" cerebral edema associated with its use. No serious complications have been reported to our knowledge with use of the urea washout test. However, since it is generally considered that the differences in medium excretion seen after infusion of urea result from an increase in urine volume on the noninvolved or less severely involved side, we decided to accomplish diuresis in the present study through use of the nonreabsorbable osmotic diuretic mannitol. This material was selected for trial on the basis of its low toxicity and potent diuretic effect. The question of the relative effectiveness of mannitol as compared to urea for detection of abnormalities in excretion of water and solute produced by functionally significant renal artery stenosis was not evaluated in this study.

Nine of our 16 patients having hypertension resulting from renal artery stenosis showed unilateral delayed appearance of medium on the affected side on either the 2 minute or the 3 minute film in the minute sequence series, while all 16 patients having primary hypertension gave a normal response to this test.

Results of the mannitol washout test were positive in 13 of the 32 cases which are the basis of this report. In 3 cases the results were classed as false-positive because distinct unilateral washout appeared when no functionally significant renal artery stenosis was present. A false-positive

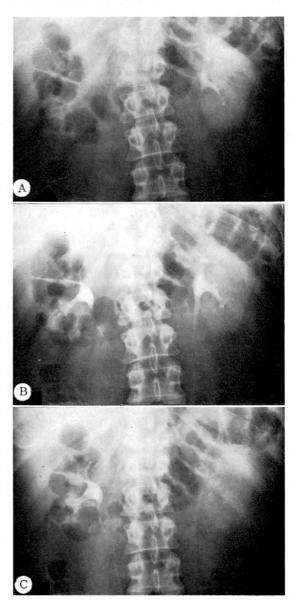
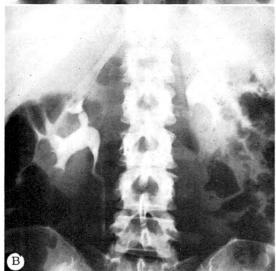
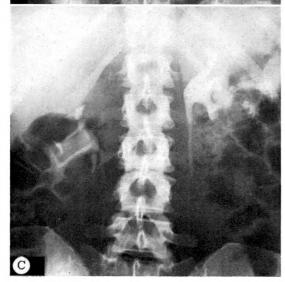


Fig. 3. Case 28. Renovascular hypertension—severe stenosis of right main renal artery. (A) Positive result on right on minute sequence urogram (3 minute film). (B) Five minute urogram made just before start of mannitol infusion. (C) Positive result on right on mannitol washout test.

result was obtained in 2 cases of primary hypertension and in 1 case of functionally significant stenosis of an aberrant left renal artery. Conversely, and in contrast to the already mentioned observations of Schreiber *et al.* with respect to the urea washout test,⁵ the result of the mannitol washout







test was negative in 5 cases of functionally significant renal artery lesions. One of these patients had bilateral disease while the other 4 had severe unilateral renal artery stenosis.

SUMMARY AND CONCLUSIONS

None of the presently available urographic techniques provides more than strong suggestive evidence for the possible presence of renal artery stenosis causative of hypertension. Disparity in renal size, "spasticity" of calyces, and retention of medium may be helpful in diagnosis in occasional cases; but they are not reliable indicators of functionally significant renal artery stenosis. Increased concentration of medium is a useful sign, but it is frequently difficult to interpret with certainty and is seen in only a relatively small proportion of cases.

Minute sequence urography appears to be the most practical urographic technique available for study of these cases as this examination is easily performed as part of the routine excretory urogram. Barring urinary tract obstruction or severe unilateral parenchymal disease, a disparity in the time of appearance of the medium is strong evidence for functionally significant renal artery stenosis.

Osmotic diuresis achieved with a non-reabsorbable osmotic diuretic agent (mannitol washout test) is of assistance in diagnosis in some cases, when the minute sequence urogram fails to demonstrate a disparity in the appearance time of the medium; but our experience in this series suggests that this examination is not a satisfactory substitute for separated renal

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Fig. 4. Case 24. Renovascular hypertension—severe stenosis of left renal artery. (A) Negative result on minute sequence urogram (3 minute film). (B) Five minute urogram, just before start of mannitol infusion. (C) Positive result on left on mannitol washout test.

function studies or for other functional parameters available for detection and diagnosis of hypertension of renovascular origin and that undue reliance on this procedure alone for detection and diagnosis of hypertension of renovascular origin is hazardous since both false-positive and false-negative results occur in a significant proportion of cases.

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THE ROENTGEN DIAGNOSIS OF RENAL VEIN THROMBOSIS*

CLINICAL ASPECTS

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THE clinical response of patients to renal vein thrombosis is variable. Blood chemistry and urinalysis may or may not show renal dysfunction. Most of the findings are nonspecific and do not indicate the etiology or the site of the circulatory disturbance in the kidney. Scattered reports in the literature and the data of animal experiments indicate that the different roentgenologic examinations of the urinary tract are of considerable value in the diagnosis of renal vein thrombosis.

The purpose of this paper is to present 5 cases of renal vein thrombosis with emphasis on the role of excretory urography, inferior vena cavography, selective renal phlebography and renal angiography. For clearer understanding of the disease, a morphologic staging is proposed.

REPORT OF CASES

CASE I (A.G. G-NHC H-59-85-61). This 74 year old man was admitted to the hospital because of chest pain which was related to a steering wheel injury sustained 6 months previously. He was otherwise asymptomatic. Urinalysis showed normal findings except for traces of albumin. In the course of his evaluation, an angiocardiogram excluded the clinical question of pericardial tamponade. The renal outlines could not be seen in the postangiographic pyelogram. There was no excretion of contrast material by the right kidney. A subsequent excretory urogram (Fig. 1A) showed no excretion on the right. The left kidney was slightly enlarged. The collecting system was normal. In addition, there was an irregular contour to the left mid-ureter. Translumbar aortorenal angiography showed a right renal tumor.



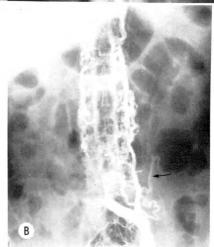


Fig. 1. Case I. (A) Excretory urogram demonstrates no excretion by the ill-defined right kidney. The slightly enlarged left kidney shows normal function. A narrowing is noted in the left mid-ureter at the level of the 5th lumbar vertebral body. (B) Inferior vena cavogram shows tumor thrombosis of the inferior vena cava and extensive venous collaterals. Of interest is the ureteric vein which caused an extrinsic pressure defect on the left mid-ureter seen in the intravenous pyelogram.

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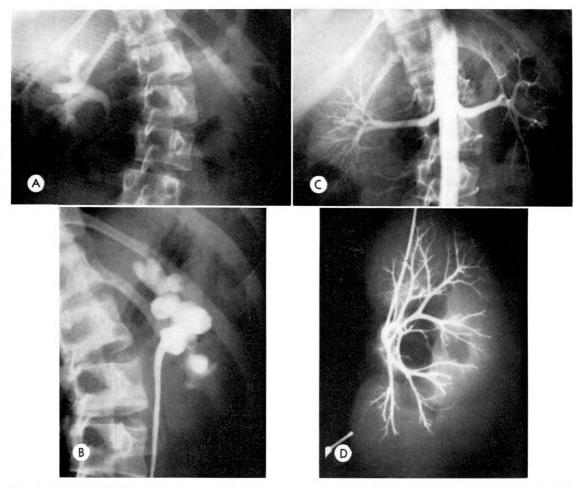


Fig. 2. Case II. (A) Intravenous urogram shows a normal right kidney and a large nonfunctioning left kidney. (B) Retrograde pyelogram shows on the left mild caliectasis with disproportionate increased thickness of the renal parenchyma. (C) Transfemoral aortorenal angiogram demonstrates delayed flow of medium in the left kidney with an abnormal arterial pattern characterized by splaying and displacement of vessels. (D) An arteriogram and air pyelogram of the resected left kidney shows subcapsular hemorrhage at the outer lower pole. The pathologic diagnosis was renal vein thrombosis, principally of the small veins and venules at the corticomedullary junction.

The angiographic pattern of the left kidney was normal. The venous drainage of the kidneys was not seen. An inferior vena cavogram (Fig. 1B) demonstrated complete occlusion of the inferior vena cava with drainage via venous collaterals. A vein, which filled by reflux from the iliac system, was visualized along the course of, and indented the, left mid-ureter.

Occlusion by tumor of the right renal vein was observed at surgery. The inferior vena cava was hard and nodular. Numerous collateral veins were seen draining the right kidney. One vein, which may have been the ureteric vein, was distended but pliable and located lateral to the inferior vena cava. The pathologic diagnosis was carcinoma of the right kidney invading the right renal vein which extended into and occluded the inferior vena cava.

Case II (R.L. G-NHC-H-59-51-07). The abrupt onset of left flank pain prompted this I5 year old female to consult her family physician. Urinalysis showed no abnormal findings. An intravenous pyelogram (Fig. 2A) revealed a normal right kidney and an enlarged left kidney without evidence of function. A retrograde pyelogram (Fig. 2B) showed mild caliectasis and dilatation of the proximal renal pelvis. The

distal renal pelvis was poorly visualized. An aortorenal angiogram (Fig. 2C) demonstrated the right kidney to be normal. On the left, a decrease in the rate of flow of the contrast material was seen. The major intrarenal branches were spread and the small intraparenchymal branches were not well visualized. The nephrogram was less dense than on the right. No venous filling was observed. Although the findings were similar to those noted in hydronephrosis, the possibility of renal vein thrombosis was strongly considered because of the acute onset and the thickened renal parenchyma which was out of proportion to the degree of hydronephrosis.

At surgery, the left kidney was enlarged and its capsule was edematous with hemorrhagic foci. There was approximately 15 cc. of subcapsular hemorrhage (Fig. 2D). The upper pole was normal in consistency and color. The lower pole was softer and cyanotic. The renal pelvis above the renal vein was dilated. Pathologic examination demonstrated variable aged thrombi (fresh and organized) in the small veins and venules at the corticomedullary junction.

CASE III (G.D. CGH-92981). An 18 year old normotensive, white female with ascites was referred to the Radiology Department for evaluation of the splenorenal shunt. This had been established several years prior to the present admission, for bleeding esophageal varices due to portal hypertension. Urinalysis revealed mild pyuria and albuminuria. An intravenous pyelogram was normal. Filling of the left ureter was incomplete so that evaluation for ureteric varices on this examination was not possible. Inferior vena cavography was normal. Selective renal phlebography was undertaken with normal findings on the right side. The left renal vein could not be catheterized, which suggested that it was occluded.

Selective left renal angiograms (Fig. 3, A, B and C) showed the arterial and nephrographic patterns to be normal. The renal vein did not opacify. However, a dilated and tortuous ureteric vein filled. The diagnosis of left renal vein thrombosis with occlusion of the splenorenal shunt was made.

CASE IV (P.G. G-NHC H-55-30-14). A 43 year old white female had been followed for 12 years by the Urology Service because of 5 epi-

sodes of intermittent, painless hematuria. Urinalysis was normal except for the intermittent evidence of hematuria. Intravenous (Fig. 4A) and retrograde pyelograms on several occasions have been interpreted as normal. Cystoscopy during several episodes of hematuria revealed blood to be coming from the left ureter.

Selective right renal angiography was normal. On the left, the arterial and nephrographic phases were also normal. During the venous phase, there was opacification of the ovarian vein which drained inferiorly toward the pelvis (Fig. 4, B and C). Selective left renal phlebograms (Fig. 4, D and E) showed a filling defect in the renal vein. Small abnormal veins were visualized draining superiorly. The left ovarian vein, which was seen in the late phase of the arteriography, was again opacified. In view of the clinical history, renal vein thrombosis with recanalization and collateralization was the diagnosis of choice.

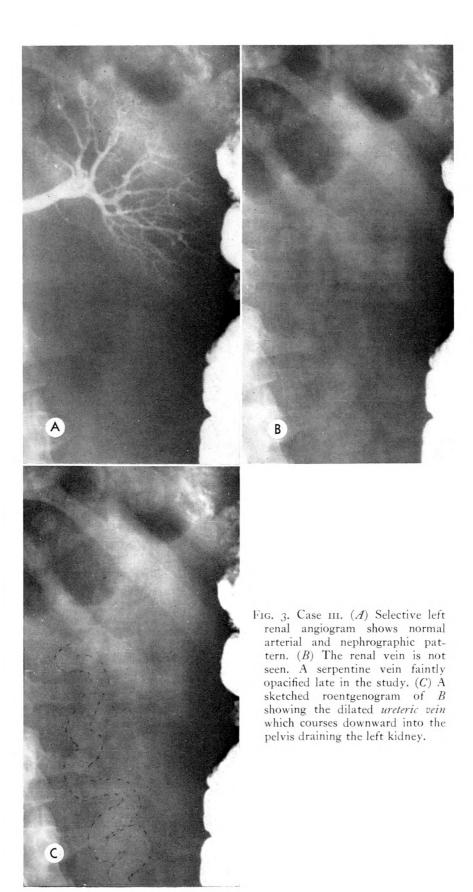
Case v (D.G.H., #142098). This 59 year old white male had an aortic bifurcation graft for severe atherosclerotic disease 2 years ago. He did well until about 3 months prior to this when he experienced the insidious onset of right leg claudication. Urinalysis on both admissions was unremarkable.

Angiographic evaluation of the aorta and the lower extremity vessels was done by reflux aortography. Fifty cubic centimeters of 50 per cent hypaque were injected through a teflon needle in the left femoral artery after the Valsalva maneuver had been sustained for 12 seconds. The aortic prosthesis was noted to be in excellent condition. Moderate atherosclerotic change in the vessels of the pelvis was seen (Fig. 5A). The right superficial femoral artery was occluded at the adductor canal with poor run-off. The vessels of the left lower extremity showed no significant change. Both renal arteries appeared normal. The left renal vein was not identified in the venous phase of the angiography. Instead, a dilated ureteric vein was opacified (Fig. 5B).

Review of the excretory urogram made before the placement of the aortic graft showed a normal left ureter. An intravenous pyelogram, 2 weeks postoperatively, showed scalloping of the left ureter, indicating the presence of ureteric varices (Fig. 5C).

Our impression was left renal vein thrombosis which may have been the result of trauma to

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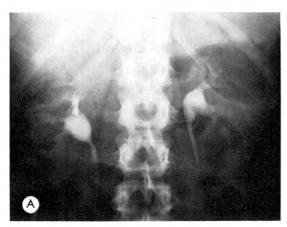


Fig. 4. Case IV. (A) Normal excretory urogram in a patient with intermittent painless hematuria.

the renal vein during surgery. The major venous drainage of the kidney was now via the ureteric vein.

DISCUSSION

Renal vein thrombosis may occur spontaneously or as a complication of various conditions such as renal neoplasms, amyloidosis, trauma, papillary necrosis, pyelonephritis and dehydration. The clinical picture, which may be difficult to distinguish from that of the underlying condition, is related to the rapidity of the venous occlusion. With rapid occlusion, marked engorgement results in capsular distention and hemorrhagic infarction. Renal rupture may lead to retroperitoneal hemorrhage. The clinical picture is that of flank pain and an enlarged, tender kidney. In cases of rupture, hemorrhagic shock and death may ensue. On the other hand,

$T_{\rm ABLE~I}$ potential renal vein collaterals

- Renoazygos
- 2. Gastrorenal
- 3. Adrenolumbar
- 4. Inferior phrenic
- 5. Adrenorenal
- 6. Splenorenal
- 7. Renolumbar
- 8. Gonadal
- 9. Ureteric
- 10. Renosystemic

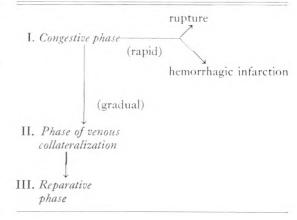
when venous occlusion is gradual, the renal engorgement is minimal. Then clinical symptoms may be absent and the kidney remains viable.

Hemorrhagic renal infarction results in total loss of function. Functional derangement may be transitory in cases of gradual occlusion. Urinalysis performed at an appropriate time may show hematuria, albuminuria or pyuria. After the congestive phase, the urinalysis may be normal as it will be with unilateral involvement in which loss of function has occurred. Hematuria has been reported in instances of ureteric varices and can be a late complication of renal vein thrombosis (Case IV). One patients with bilateral or even unilateral involvement may develop the nephrotic syndrome.

Following renal vein occlusion, the venous drainage is via a potentially extensive collateral network (Table 1). The balance between the speed with which this collateral system can develop and the rapidity of the occlusion is critical in determining the outcome of any individual case.⁴

Because of the spectrum of response of the kidney to occlusion of the venous drainage and the varied functional outcome in each individual, we believe that it is helpful to consider renal vein thrombosis as a series of stages (Table II).

TABLE II
PROPOSED MORPHOLOGIC STAGING



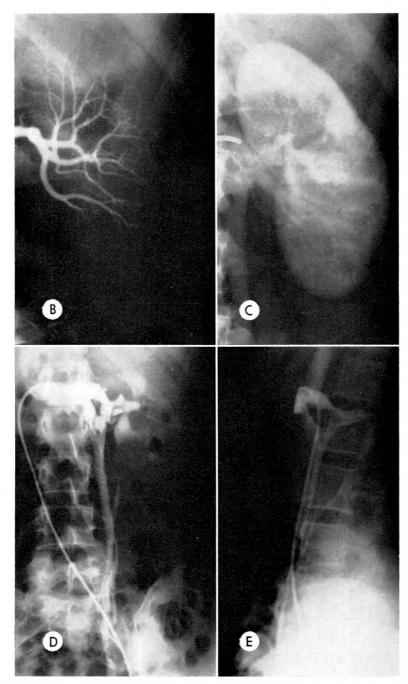


Fig. 4. (B and C) Likewise, the renal arteriographic and nephrographic phases are normal. The renal hilar veins were opacified with retrograde filling of the left *ovarian vein*. (D and E) Selective left renal phlebograms show an irregular filling defect in the small renal vein. Numerous small abnormal veins are seen in the region of the renal hilus. The ovarian vein drained toward the pelvis.

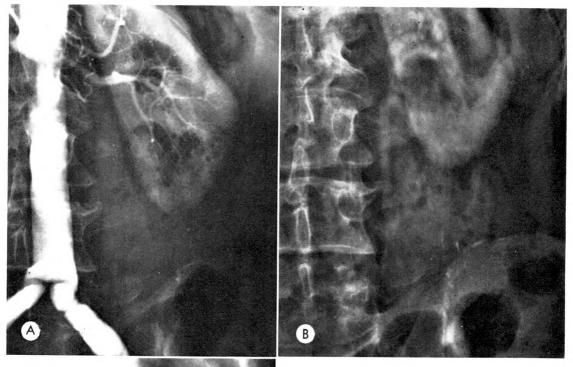




Fig. 5. Case v. (A) Reflux transfemoral aortorenal arteriogram demonstrates patency of the abdominal prosthesis and a normal arterial supply to the left kidney. (B) The venous phase of the preceding aortogram shows no opacification of the main renal vein. The venous drainage of the left kidney was now via collaterals, particularly the ureteric vein. (C) Postoperative excretory urogram, which was previously normal, exhibits extrinsic pressure undulations on the left ureter from venous collaterals.

Recent reports in the literature have emphasized the role of roentgenologic examinations in the diagnosis of renal vein thrombosis. In addition, animal experiments have shown that roentgen examination is very helpful in the evaluation of renal vein thrombosis.^{2,4}

EXCRETORY UROGRAPHY

The various pyelographic appearances in renal vein thrombosis reported in the literature fail to reveal a specific picture. This is not surprising in view of the rapid change in the kidney as the collateral circulation develops.4 Rapid occlusion of the renal vein will result in congestion and considerable enlargement of the kidney. If hemorrhagic infarction ensues, function will be lost and atrophy will take place. If venous obstruction is gradual and collateral circulation develops, function may be preserved. The kidney will return to almost normal size although slight enlargement may persist. Therefore, a variable sized kidney with normal or impaired excretion of contrast may be seen in renal vein thrombosis.

Zheutlin *et al.*¹³ likened the distortion of the collecting system to that seen in polycystic disease of the kidney. These changes are observed only in the congestive phase of renal vein thrombosis. Thus, the kidney is enlarged but the over-all renal outline is not lobulated as seen in polycystic disease.

The dilated collaterals of the ureteric venous plexus may cause extrinsic pressure defects on the ureter, resulting in a notched or scalloped appearance (Cases I and V). Such a change has been observed experimentally⁴ and clinically.^{1,2,3,5,12} However, the notched or scalloped appearance of the ureter is not pathognomonic of ureteric varices. Dilatation of the ureteral artery has been noted to produce similar changes in the contour of the ureter.^{7,9} Historical data and arteriography will differentiate these two conditions.

INFERIOR VENA CAVOGRAPHY

Inferior vena cavography has been re-

ported to be useful in the diagnosis of renal vein thrombosis.⁸ In the case of complete obstruction of the vena cava, the renal venous drainage, of necessity, is by way of collaterals (Case I). If the vena cava is not completely obstructed but thrombi are detected, particularly in the region of the renal vein orifices, or if no dilution defects are noted near the entrances of the renal veins, one may infer that thrombi are present in the renal veins.

At the time of vena cavography, the Valsalva maneuver may be utilized to reflux contrast material into the renal veins. Good reflux will demonstrate patency of the lumen or may even outline a partially obstructing thrombus. The absence of reflux does not necessarily imply occlusion because we have observed this phenomenon in instances where other studies have demonstrated patency.

RENAL PHLEBOGRAPHY

March and Halpern¹¹ and Eisen et al.⁵ recently reported the use of selective renal phlebography in renal vein thrombosis. By this method of examination, the presence of thrombi in the renal, gonadal and adrenal veins has been demonstrated and the collateral venous drainage has been opacified. In instances of complete occlusion, catheterization of the vein will not be possible and this may be presumptive evidence of obliteration of the lumen (Case III). A false negative examination might result if the thromboses were in the smaller renal veins or venules (Case II). Incomplete opacification of the renal vein or collaterals may occur because of streaming of the contrast material which is injected countercurrent. A very forceful injection may reverse hemodynamics and give a false impression. Moreover, there is a possible danger of dislodging a piece of thrombus with resultant embolization. These problems do not arise with arterial injection of the contrast medium.

Beres *et al.*² have described the use of percutaneous transrenal venography in the diagnosis of renal vein thrombosis. We have

no personal experience with this method. The published illustrations show excellent opacification of the venous collaterals. The disadvantage of this method, which is inherent in any blind puncture of a highly vascular organ, is the possibility of severe hemorrhage.

RENAL ANGIOGRAPHY

Renal angiography is of considerable value in the diagnosis of renal vein thrombosis. Serial filming must be programmed to cover the entire kidney circulation, particularly in the venous phase which normally occurs 10 to 15 seconds after the start of injection. As with the other methods of investigation, the angiographic picture will depend upon the stage of the disease. In the enlargement or congestive stage, the arterial pattern will show decrease in caliber with spreading of the small intraparenchymal branches. The finer intraparenchymal branches may not be seen. The flow of the contrast material is delayed and the nephrographic density is decreased (Case II). Although the appearance is similar to that seen in hydronephrosis,^{1,18} the thickened renal parenchyma will be in favor of renal vein thrombosis.

If renal viability is preserved, the collateral venous drainage may be opacified in the later phase of the study (Case III).⁴ This is best demonstrated with a selective renal artery injection rather than an injection into the aorta. The alterations in the arterial and nephrographic phases bear an inverse relationship to the development of the venous collaterals.

The arterial and nephrographic pattern may be normal with the exception of decreased opacification of the very small intrarenal branches when the venous circulation is well developed. The pattern of the venous drainage and direction of blood flow from the kidney can be determined. The opacification of collaterals in the absence of, or partial visualization of, the renal vein will allow one to make the diagnosis of renal vein thrombosis.

COMMENT

The selection of the proper examination will depend upon the clinical circumstances in the individual case. The simplest examination is intravenous pyelography. If the femoral vein is used for injection, inferior vena cavography can be done prior to excretory urography, utilizing the same contrast material. Renal angiography is the most informative of the special procedures and should be considered early in the evaluation of suspected cases of renal vein thrombosis.

SUMMARY

- 1. Five cases of renal vein thrombosis are reported. Cases I and II are histologically proven. Presumptive diagnosis of renal vein thrombosis is made in Cases III, IV and V on the basis of angiographic criteria in the light of previous experience and experimental evidence.
- 2. The clinical aspects and laboratory findings are briefly considered.
- 3. The manifestations of renal vein thrombosis as seen at the time of excretory urography, inferior vena cavography, selected renal phlebography and renal angiography are discussed.
- 4. Renal angiography is the most valuable examination because the changes in the different phases of the renal circulation can be demonstrated.
- 5. A morphologic staging of renal vein thrombosis based on the pathophysiology of the disease is proposed.

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RENAL ARTERY ANEURYSMS*

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RENAL artery aneurysms are said to be relatively rare. In 1962, Milton¹⁰ compiled only 143 cases from the English literature. Boijsen and Köhler,³ in 1963, reported 12 cases, the largest series reported from any single institution. It has been estimated that there have been about 200 cases published in the world literature. The autopsy incidence has been reported as 1 per 8,000 by Begner² and 1 per 10,000 by Ippolito and LeVeen.⁷

MATERIAL

We have recently reviewed the experience at Duke University Medical Center with this disease entity and found a total of 25 cases. Twenty of these cases have been diagnosed antemortem while 5 have been discovered at postmortem examination. The autopsy incidence was I per 2,400.

This series of cases are subdivided into 3 categories in respect to their associated clinical findings (Table 1). In Group 1 are the patients who were hypertensive and whose aneurysm was discovered as part of their hypertensive studies (76 per cent). In Group 11 are the patients whose aneurysms ruptured with subsequent retroperitoneal hemorrhage (8 per cent). In Group 111 are those patients whose aneurysms were incidentally discovered during other roent-genographic studies (16 per cent).

When the age, sex and race of these patients are compared, two rather unusual pieces of information become apparent. Twelve of the 25 patients (48 per cent) were white females, while our hospital admission rate indicates that only 37 per cent of the total admission are white females.

TABLE I
ASSOCIATED CLINICAL FINDINGS

Group	No. of Patients	Per Cent		
I. Hypertension II. Hemorrhage III. Incidental	19 2 4	76 - 8 16		
Total	25	100		

In addition, there was a bimodal distribution with 25 per cent of the patients in the 20–29 year old age group and 25 per cent in the 50–59 year age group. These peak incidences are not related to the incidence of arteriosclerotic and nonarteriosclerotic changes found in the pathologic specimens.

DIAGNOSTIC FEATURES

The diagnosis of renal artery aneurysms may be suspected in plain roentgenograms only when the aneurysm is calcified. The type and configuration of the calcification in these aneurysms have been well described. The incidence of calcification in this type of aneurysm has been reported at 27 per cent by Ippolito and LeVeen⁷ and 50 per cent by McLelland. In the total group of cases with renal artery aneurysms, 9 out of 25 (36 per cent) had roentgenographically visible calcification. If, however, only the 16 proved cases are considered, 6 (43 per cent) of these patients had aneurysms with visible calcification.

The presence of visibly calcified aneurysms on plain roentgenograms is no real indication of the total number of aneurysms in any given patient. When only the patients who have had aneurysms proven by angiography or surgery are considered,

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there were 6 patients with calcified aneurysms. These 6 patients had a total of 7 calcified aneurysms. Moreover, and probably more important, there was a total of 12 aneurysms found in these 6 patients. This series of patients, although small in number, would indicate that there may be many more aneurysms present than visible on plain roentgenograms.

The presence of multiple aneurysms is an important point in the over-all care of the patient. Boijsen and Köhler³ quote several authors regarding hemorrhage and then draw the following conclusion. "None of the many case reports in the literature mentions rupture of a calcified aneurysm. Thus, apart from pregnancy, calcified aneurysms do not indicate immediate surgery." From one aspect we would agree with this quotation; calcified aneurysms probably do not hemorrhage. However, from another aspect, the quotation from Boijsen and Köhler may well be too complacent, since an analysis of the presently reported small group of well documented aneurysms would indicate that a patient may have noncalcified aneurysms coincident with calcified ones. The mere presence of calcification, typical of an aneurysm, should not imply that this patient cannot hemorrhage. Angiography is required for complete evaluation as to the total number of aneurysms present in any given patient.

Our experience with renal artery aneurysms would indicate that there is a closer relationship between this type of aneurysm and hypertension than has been reported in the literature. Table I shows that 19 out of 25 patients (76 per cent) had documented hypertension, while Ippolito and LeVeen reported only a 19 per cent and Boijsen and Köhler only a 15 per cent incidence. In addition, Milton¹⁰ has expressed the opinion that aneurysms are coincidental to hypertension and that there is an associated stricture or thrombus in the vessel adjacent to the neck of the aneurysm. He went further to tabulate an inverse relationship between the level of the blood pressure and the diameter of the lumen of the

vessel at the thrombus or stricture. Our series of cases would indicate that aneurysms without associated strictures, thrombus or renal parenchymal disease may produce sufficient alteration in renal hemodynamics to account for a "Goldblatt" phenomenon. The manifestations of altered hemodynamics are also a very valuable diagnostic sign and are seen with aneurysms in various vessels. Aneurysms of vessels first may cause a delay in filling of the vessels beyond them and, secondly, retain contrast material long after the adjacent vessels have lost their contrast material. Aneurysms may also cause incomplete filling or sparse visualization of the parenchymal vessels throughout the kidney. The following 2 cases are examples of such phenomenon.

ILLUSTRATIVE CASES

Case I (Fig. I, A-D). This 49 year old white female had a history of hypertension of I year's duration. The angiographic study showed bilateral renal artery disease with arteriosclerotic changes on right, fibromuscular changes of the left renal artery and an aneurysm at the bifurcation on the left. Figure IA shows the aneurysm with early swirling of contrast material around its edge. Figure IB shows filling of the aneurysm with lack of filling of the vessels beyond the aneurysm. Figure IC shows better filling of the aneurysm and the vessels beyond it. Figure ID shows contrast material in the aneurysm after the vessels have been "washed out."

CASE II (Fig. 2, A and B). This 25 year old white female had documented hypertension and an aneurysm at the bifurcation of the right renal artery. Figure 2A is the preoperative angiogram and Figure 2B the postoperative arteriogram of the surgical specimen. The pathologist found no evidence of primary renal disease and no stricture or thrombus in the vessel.

Comment. Of 8 hypertensive patients in our series whose aneurysm required nephrectomy (Table II), there were 4, who on review of the operative notes, gross specimen pathology reports, and the tissue sections were found to have no associated

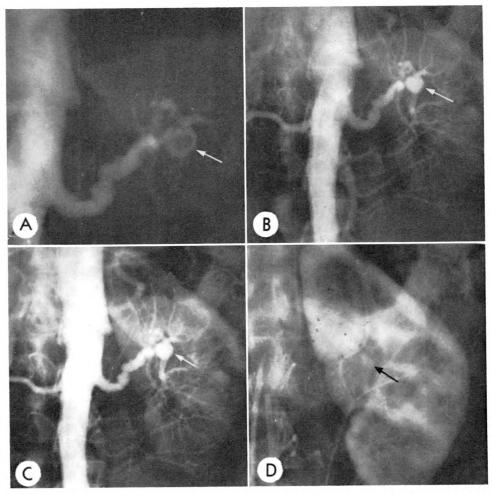


Fig. 1. Case 1. (A) 0.25 sec. Fibromuscular hyperplasia of left renal artery and aneurysm at the bifurcation. The aneurysm has a ring-like configuration since the contrast material is swirling around the edge. (B) 0.5 sec. The aneurysm is now homogeneously dense. Small branch arteries beyond the aneurysm are not visualized while similar sized arteries in upper and lower pole are visible. (C) 0.75 sec. The smaller branch arteries are now evenly filled. (D) 2.5 sec. The aneurysm retains contrast material while the adjacent vessels are "washed out."

 $\label{eq:Table II} Table \ II$ methods of treatment (all cases)

Treatment	No. of Cases		
Nephrectomy	10	(2) 8)
Aneurysmorrhaphy	I	(Incidental	1)
No Surgery	14 (Hypertensive (Incidental		1) 3)

intrarenal disease. In addition, there was no evidence of stricture or thrombus in the arteries. Of these 4 patients, 3 have remained normotensive for 15 months to 6 years following surgery. The other patient was markedly improved. Furthermore, of the 8 patients, 6 (75 per cent) have remained normotensive for longer than 1 year, 1 patient (12 per cent) has been markedly improved, and 1 patient had a recurrence 3 months following nephrectomy. It seems feasible that an aneurysm may pro-

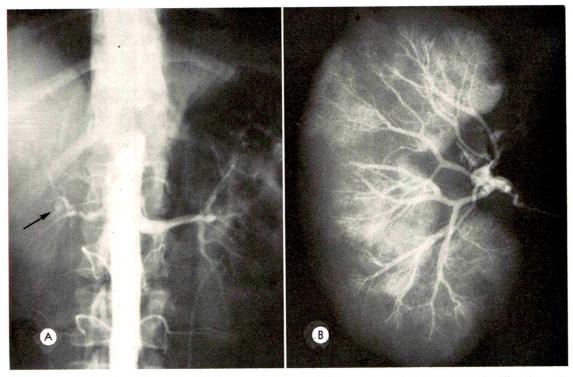


Fig. 2. Case II. (A) One film from serial renal aortography. The aneurysm is homogeneously filled (arrow). The vessels throughout the right kidney are sparse and narrow in diameter. This vascular pattern was present throughout the study. (B) Arteriogram of the surgical specimen. The aneurysm is visualized. The vascular pattern throughout the kidney is normal.

duce sufficient alteration in the blood supply to cause hypertension.

CONCLUSION

- 1. Since patients with calcified renal artery aneurysms may also have noncalcified aneurysms, the presence of calcification in a renal artery aneurysm does not, in itself, exclude the possibility of serious retroperitoneal hemorrhage from the noncalcified aneurysms.
- 2. It is feasible that an aneurysm alone, without associated stricture or thrombus in the vessel and without associated intraparenchymal renal disease, may well be sufficient to produce renovascular hypertension.

William F. Barry, Jr., M.D. Department of Radiology Duke University Medical Center Durham, North Carolina The microscopic sections on these cases were reviewed by Dr. Stanley M. Kurtz, staff member of the Department of Pathology at Duke University Medical Center, who was kind enough to give his time to help us with this review.

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ANGIOGRAPHY OF RENAL AGENESIS AND DYSGENESIS

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ITH the advent of renal angiography, a new modality was added to techniques used in evaluating the nonfunctioning kidney. We have employed arteriography routinely in cases where the etiology was not immediately apparent by the usual roentgenographic procedures. One rare cause of nonvisualization is the case of a solitary kidney. The incidence of solitary kidney, according to Eisendrath,3 varies between 1:400 to 1:4,000, but Meyer et al.4 of Peter Bent Brigham Hospital feel that 1:1,000 is a more acceptable figure. The discrepancy probably results from the failure of most authors to differentiate between agenesis, dysgenesis and hypoplasia.

According to the classification of Ashley and Mostofi,² the anomaly is considered agenesis if no vestige of renal tissue is detected; if the kidney is represented by a nodule of tissue bearing no morphologic or histologic resemblance to normal renal parenchyma, it is designated dysgenesis, while the term of hypoplasia is reserved for cases having a kidney that is small but otherwise similar to the normal organ.

The developmental anatomy of the kidnev and ureter is helpful in understanding the differentiation between agenesis and dysgenesis.1 The wolffian or mesonephric duct drains the mesonephros. It grows caudally and reaches the cloaca, which will eventually form the bladder and rectum. As this occurs, a small bud appears on the dorsal surface of the wolffian duct a short distance above the cloaca. This bud eventually forms the ureter, growing upward and forming the anlage of the kidney proper by growing into a mass of undifferentiated mesoderm. The collecting system is thus formed by the original ureteral bud, and the kidney parenchyma arises from the

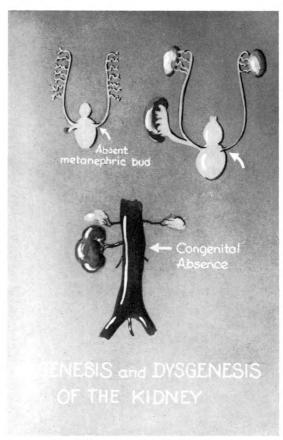


Fig. 1. Embryology of renal agenesis.

mass of mesenchyme (Fig. 1).

Should the wolffian duct fail to descend, there would be no ureter or associated part of the trigone. However, according to Ashley and Mostofi,² the metanephric blastoma has the potential for differentiation into a kidney, although without the necessary drainage for function. They state that in 108 autopsies in which the renal vessels were evaluated no cases were found in which a major renal vessel was seen with an absent or grossly deficient kidney.

In unilateral agenesis the ureter is usually absent or only a small portion of the

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Fig. 2. Case I. Intravenous pyelogram using a double dose of contrast medium demonstrates a large right collecting system with no function on the left

distal ureter is seen. The ureter was never found extending as high as the usual anatomic position of the kidney.

In unilateral dysgenesis the ureter was usually seen to be of normal length.

Three cases of unilateral renal agenesis

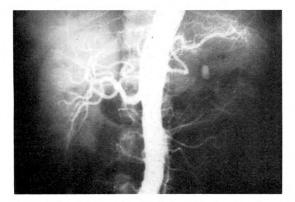


Fig. 3. Case I. Aortogram (1\frac{3}{4} sec.) shows a large right renal artery with normal branching and no evidence of a left renal artery or collaterals.

and one of dysgenesis were studied by means of aortography using the Seldinger technique. There was no evidence of a renal artery or even a bud in the cases of agenesis. In the single case of dysgenesis, a small, smooth, rounded bud was demonstrated in the usual anatomic position of the renal artery.

REPORT OF CASES

Case 1 (Fig. 2 through 4). J. B., a 39 year old Negro male, entered Cook County Hospital with a 2 week history of dyspnea on slight exertion and the clinical finding of congestive heart failure. His blood pressure was 210/130. An intravenous pyelogram showed failure of function of the left kidney and a large right kidney. An aortogram, using 40 cc. of sodium iothalamate 66.8 per cent, demonstrated a single large right renal artery and no evidence of a left renal artery, bud or collaterals. Cystoscopic examination showed absence of the left half of the trigone. The diagnosis was renal agenesis.

Case II (Fig. 5 through 8). N. K., a 49 year old Negro male, with a history of syphilis at the age of 17 years, had been admitted on several occasions for congestive heart failure due to luetic aortitis with aortic stenosis. His blood pressure was 110/9c. His urinalysis showed innumerable red blood cells per high power field which could not be explained clinically. An intravenous pyelogram revealed a large left kidney with minimal chronic pyelonephritic changes. Cystoscopic examination showed an

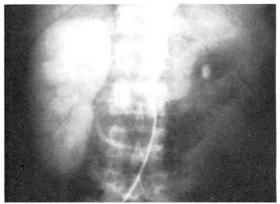


Fig. 4. Case 1. Solitary right nephrogram (8 sec.) with no evidence of delayed collaterals in the left renal area.

absence of the right side of the trigone. A retrograde aortogram showed 2 renal arteries on the left side with changes of the peripheral vessels, compatible with chronic pyelonephritis. No right renal artery, bud, or collaterals were demonstrated. The diagnosis was renal agenesis.

Case III. (Fig. 9 through 11). C. B., a 27 year old Negro female, had a 5 year history of high blood pressure related to her third and last pregnancy. Her blood pressure had risen over the years despite antihypertensive medication; it was 200/80. She has had frequent mild episodes of epistaxis. The intravenous pyelogram showed failure of function of the right kidney. At cystoscopic examination, a catheter was passed up the right ureter to the level of L-4, at which point the contrast material returned into the bladder and no upper collecting system was demonstrated. A renal angiogram showed a normal left renal artery with minimal enlargement of the left kidney. A small rounded, smooth, 2 mm. bud was seen projecting in the



Fig. 5. Case II. Intravenous pyelogram (15 min.) shows an absent right renal shadow with failure of visualization of the right collecting system and hypertrophy of the left kidney with mild chronic pyelonephritic changes.



Fig. 6. Case II. Retrograde aortogram ($\frac{3}{4}$ sec.) shows 2 left renal arteries and no evidence of a right renal artery.

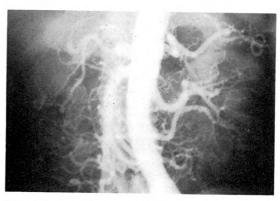


Fig. 7. Case II. Retrograde aortogram (2 sec.) shows same finding with extensive branching of the superior mesenteric artery to the right. There is a mild cork-screw appearance of the small vessels of the left kidney.

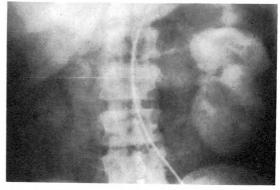


Fig. 8. Case II. Left solitary nephrogram (13 sec.) with evidence of cortical scarring and no collateral circulation on the right.

usual anatomic position of the right renal artery.

At surgery, the ureter was found ending in a



Fig. 9. Case III. Right retrograde pyelogram shows a catheter extending to the level of L-3, with contrast material I cm. above the tip of the catheter and backflow into the bladder.

blind pouch. Microscopic examination revealed a small island of renal-like tissue. The diagnosis was renal dysgenesis.

Case IV (Fig 12 through 15). B. C., a 21 year old Negro female, entered Cook County Hos-

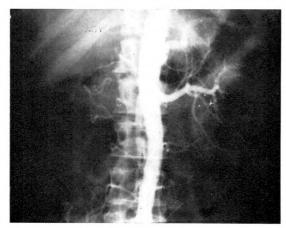


Fig. 10. Case III. Retrograde aortogram (I sec.) shows normal left renal artery and a small bud on the right.



Fig. 11. Case III. Retrograde aortogram (6 sec.) shows a solitary normal left nephrogram with no evidence of collateral flow to the right renal area.

pital with a history of hypertension which had first been noted in the last trimester of her first pregnancy. She was treated for pre-eclampsia



Fig. 12. Case IV. Intravenous pyelogram (10 min.) shows nonfunction on the left with a duplication down to the lower one-third of the ureter with pyelocaliectasis and ureterectasis on the right.

during the last trimester of her second pregnancy. Her blood pressure at that time was recorded as 180/110.

At her last admission, 4 months after her second delivery, her blood pressure was 140/90. Her heart was slightly enlarged with some prominence of the left ventricle. Urinalysis revealed 1+ albumin and occasional white blood cells.

A renogram demonstrated normal right renal function and no evidence of function on the left side.

Cystoscopy was done and only 4 inches of the left ureteral catheter was passed. Contrast material injected into the left ureteral catheter returned to the bladder.

Aortography revealed a normal right renal artery with enlargement of the right kidney and no evidence of left renal artery or collateral circulation. The diagnosis was agenesis of the left kidney with small ureteral remnant.

DISCUSSION

Arteriographically, the absence of a renal

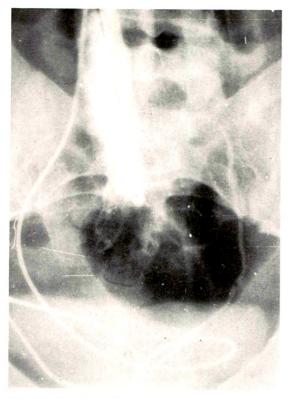


Fig. 13. Case iv. Retrograde examination reveals blind end of left ureter at level of L-4 (artefact in mid-portion of roentgenogram).



Fig. 14. Case IV. Retrograde aortogram (1½ sec.) shows a solitary renal artery and no evidence of a left renal artery or bud.

artery is seen in renal agenesis. In one case of dysgenesis, a bud-like projection was noted. This finding, together with absence of the associated half of the trigone or small persistent ureteral remnant, confirms the diagnosis of agenesis. Cases of congenital hypoplasia or occlusion of the renal artery may present a similar arteriographic appearance, but the presence of a ureter and a formed kidney on retrograde examination is sufficient to exclude the diagnosis of ageneesis or dysgenesis.

SUMMARY

- I. Three cases of unilateral renal agenesis and I of dysgenesis are reported.
 - 2. Absence of the renal artery was dem-

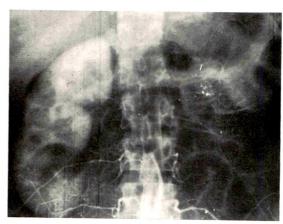


Fig. 15. Case IV. Retrograde aortogram (10 sec.) shows an enlarged right nephrogram and no evidence of a left nephrogram or collateral flow.

onstrated arteriographically in these 4 cases. No evidence of nephrograms or collaterals was noted.

3. Cystoscopic correlation with the arteriographic findings confirms the diagnosis.

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PSEUDOSTENOSIS OF THE RENAL ARTERY*

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TRANSIENT narrowing of the renal artery has been observed several times during selective renal arteriography and catheter abdominal aortography on a large group of patients. This is believed to be due to spasm of the renal artery. The appearance simulates renal artery stenosis, and therefore the term pseudostenosis seems appropriate. The diagnosis of pseudostenosis is made when narrowing of the renal artery is present on the selective arteriogram but not on the abdominal aortogram.

MATERIAL

At the University of Iowa Hospitals, selective renal arteriography was first performed in October, 1963. From then until August, 1965, selective renal arteriograms were obtained in 159 patients. In most of these, 2 renal arteries were catheterized. In a few, only 1 artery was selectively catheterized, and in a small number, more than 2 renal arteries were catheterized. Therefore, approximately 320 arteries have been catheterized. Pseudostenosis was seen in 6 renal arteries, an incidence of approximately 2 per cent.

For selective catheterization of the renal artery, a pre-curved red or green Ödman

catheter was used. Six to 10 cc. of sodium-methylglucamine diatrizoate (renovist) was injected either by hand or with the Cordis pressure injector at approximately 80 p.s.i. The abdominal aortic injections were made through a tip occluded P.E. 240 polyethylene catheter using 30 cc. of the same contrast substance with the Cordis injector at 300 p.s.i. The selective arteriogram preceded the abdominal aortogram in some cases and followed it in others.

Table I is a list of the cases showing pseudostenosis. The age of each patient, the size of the affected renal artery, the indication for, and results of, each examination are given. Figures I through 6 illustrate the findings in each patient.

DISCUSSION

There is very little in the literature concerning renal artery spasm. Haage and Rehm¹ described 2 cases demonstrated by angiography. Their first case is quite similar to our cases. In their second case a branch of the renal artery which appeared to be occluded on the angiogram was patent by histologic examination. Markland⁵ reported spasm of the renal artery at the time of surgery on the kidney, and its alle-

TABLE I

Patient	Figure	Age (yr.)	Size of Artery Showing Pseudostenosis	Indication for Procedure	Roentgenographic Diagnosis
I.S.	I, A and B	28	Normal	Recurrent urinary tract infections; renal cysts on intravenous pyelo- gram	
J.M.	2, A and B	27	Normal	Hypertension	Normal renal arteries
A.K.	3, A and B	24	Normal	Hypertension	Normal renal arteries
J.D.	4, A and B	53	Normal	Hypertension	Normal renal arteries
R.W.	5, A and B	34	Small; 1 of 2 left renal arteries	Hypertension	Normal renal arteries
C.R.	6, A and B	17	Small; dorsal branch of left renal artery	Hematuria of undeter- mined origin	Normal renal arteries

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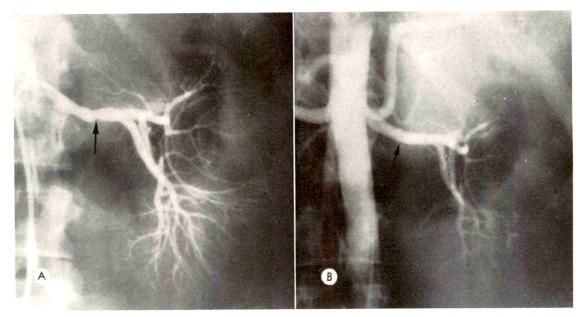


Fig. 1. I.S. (A) Selective renal arteriogram shows a discrete narrowing of the renal artery (arrow). Some of the intrarenal branches are displaced by a large cyst. (B) Abdominal aortogram. The arrow points to the site of the narrowing seen in A. The artery now is normal in caliber.

viation by topical or intra-arterial papaverine. Lindbom⁴ studied spasm in peripheral arteries during catheterization. He found that a catheter or a guide wire in the arterial lumen may provoke spasm, which

could also result from a sharp rise in intraluminal pressure. Stretching of the lumen probably results in a sudden contraction secondary to mechanical stimulation of the smooth muscle. Haage and Rehm¹ also

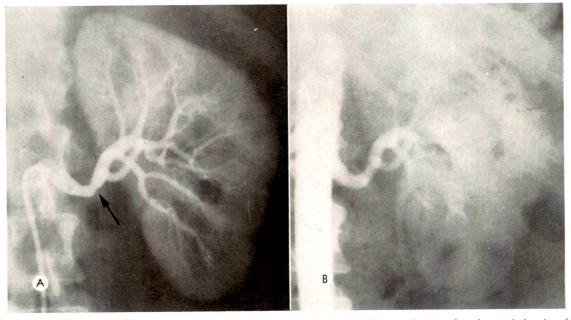


Fig. 2. J.M. (A) Selective renal arteriogram shows a narrowing of the left renal artery just beyond the tip of the catheter (arrow). (B) Abdominal aortogram. The narrowing is no longer present and the entire undivided portion of the renal artery is larger in caliber than on the selective arteriogram.

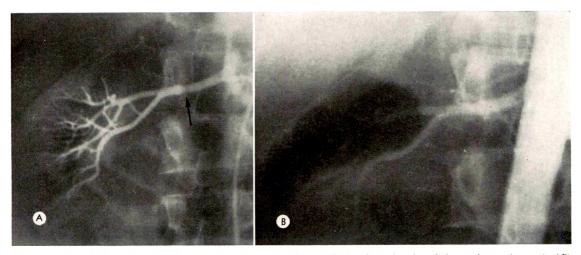


Fig. 3. A.K. (A) Selective arteriogram shows a narrowing well distal to the tip of the catheter (arrow). (B) Abdominal aortogram. The narrowing seen in A is not present.

raised the question of spasm being due to the chemical irritation of the contrast material. However, several authors^{2,5,9} have shown that present day contrast media are vasodilators rather than vasoconstrictors.

We concur with Lindbom⁴ that mechanical irritation of the catheter or of the pressure injection must be the causative factor. The small number of cases in which we have seen pseudostenosis is puzzling. Renal arteries showing pseudostenosis were not catheterized or injected in a different

manner from the ones which did not show this phenomenon. In none of the patients was pseudostenosis seen bilaterally or in more than I renal artery or branch. In reviewing Table I, several trends are noted. First of all, the renal arteries in all the patients were roentgenographically normal except for the pseudostenosis. This agrees with the experience of Lindbom who found spasm more frequently in normal vessels than in peripheral arteries with fibrotic or atherosclerotic changes. Except for I patents

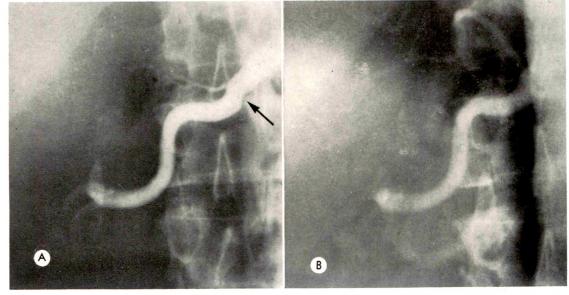


Fig. 4. J.D. (A) Selective arteriogram shows a narrowing of the renal artery at the level of the origin of an adrenal artery (arrow). (B) Abdominal aortogram. The narrowing seen in A is not present.

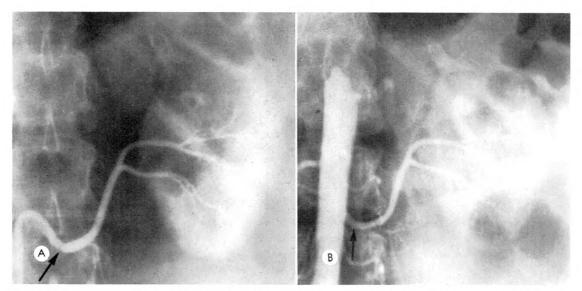


Fig. 5. R.W. (A) Selective left lower pole arteriogram. The arrow points to a narrowing just distal to the tip of the catheter. (B) Abdominal aortogram. The artery is now smooth and regular with no narrowing at the previous site (arrow).

tient, aged 53 years, all our patients were 34 years of age or under. This, too, suggests that spasm is more likely to occur in relatively young patients. The size of the artery is apparently of no importance. The preponderance of hypertensive patients

merely reflects the selection of cases for renal arteriography.

It is important for the radiologist to be aware of pseudostenosis of the renal artery. It has been recommended that hypertensive patients be studied by selective renal

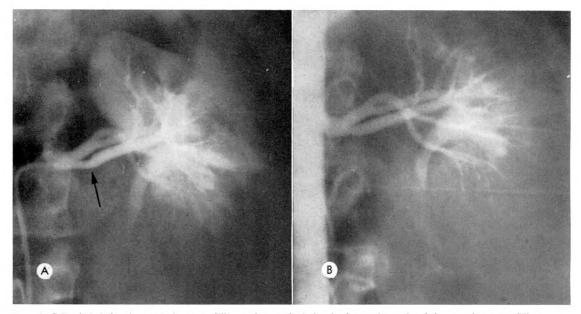


Fig. 6. C.R. (A) Selective arteriogram. The catheter tip is in the lower branch of the renal artery. The arrow points to a narrowing of this branch, slightly distal to the bifurcation. (B) Abdominal aortogram. Although there is minimal residual narrowing at the bifurcation, the previously narrowed area is no longer present.

arteriography. Selective studies frequently add useful information to the abdominal aortogram. However, abdominal aortography should always be performed if a stenosis of the renal artery is seen on the selective injection. In our opinion, abdominal aortography is the more important procedure in hypertensive patients and should be done prior to insertion of a catheter into the renal arteries for selective arteriography. This program should obviate both false positive and false negative interpretations.

SUMMARY

Pseudostenosis or spasm of the renal artery was seen in approximately 2 per cent of selective renal arteriograms in 159 patients. It is believed to be caused by the mechanical irritation of the catheter or of the injection. It occurs for the most part in younger patients whose renal arteries are otherwise normal. It is emphasized that the complete evaluation of the renal arteries requires an injection into the abdominal aorta. Selective renal arteriography may be used in addition as the case requires. Only in this manner will erroneous interpretations be minimized.

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URETEROPELVIC JUNCTION OBSTRUCTION

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TRETEROPELVIC junction obstruction is an established and often made diagnosis. Roentgenologic and surgical findings have given rise to conflicts concerning the etiology with no complete agreement on any one cause. Stenosis, valve, blood vessel and fibrotic band have been variously given as causes for the obstruction.⁵ Mayo¹⁷ mentions anomalous blood vessels as a common cause for this condition, but Hahn¹¹ states that fibrotic strictures and bands may be mistaken for anomalous vessels and reports cases of unimproved hydronephrosis following division of blood vessels which were thought at surgery to have caused the obstruction.

In 1961, Gross and Sanderson⁸ stated that ureteral and pelvic dilatation is occasionally produced by the vesicoureteral reflux phenomenon and cautioned of the high incidence of reflux in patients showing ureteropelvic obstruction on excretory urograms. In 1962, Hutch *et al.*¹³ made the observation that some renal pelves, overfilled by refluxed urine, were roentgenologically identical in appearance to "primary" ureteropelvic obstruction.

Lack of correlation between the roentgen and surgical findings is common and has been emphasized by Emmett.⁵ Jonathan and Magri¹⁶ found no obvious abnormality of the pelviureteric junction in 35 of 55 patients operated on for ureteropelvic junction obstruction. It is evident that some patients are diagnosed and operated on for a roentgenologically apparent ureteropelvic junction obstruction which does not actually exist. An explanation for this situation has been provided by a group of patients who exhibited features of the upper urinary tract resembling ureteropelvic junction obstruction, yet in whom obstruction was obviously absent.

The purpose of the author is to discuss the pathogenesis of nonobstructive renal pelvic dilatation in relationship to that caused by obstruction. A classification of the dilated renal pelvis and criteria for the various types will be presented.

MATERIAL

Thirty five patients with dilatation of the renal pelvis, typical of ureteropelvic obstruction, have been observed in over 350 examined by intravenous pyelography and cystourethrography for urinary tract infection. Twenty-nine of these had non-obstructive dilatation, whereas the remaining 6 had organic obstruction. The patients were between the ages of 2 and 10 years except for one 16 year old boy and one 18 month old girl. Four of the 29 with non-obstructive dilatation and all 6 with organic obstruction had surgical exploration.

PATHOGENESIS

NONOBSTRUCTIVE DILATATION

Renal pelvic dilatation and kinking or narrowing at the pelviureteric junction are the classic criteria which have been used in the past for a diagnosis of ureteropelvic junction obstruction (Fig. 1, A, B and C). Such an appearance is not pathognomonic of organic obstruction as shown in this study. Twenty-nine patients without obstruction exhibited features of the renal pelvis which, if considered alone, were identical to those of classic ureteropelvic obstruction (Fig. 2, A, B and C).

Generalized nonobstructive dilatation of the renal collecting system has been established as an entity by several investigators. Some believe that infection is one factor causing such dilatation, 15,18,19,21 whereas others have considered reflux as the only etiologic agent. 6,8,13 Tubular structures, such as the ureter, become tortuous and elongated as their diameter increases. The tortuosity occurs in the areas of greatest

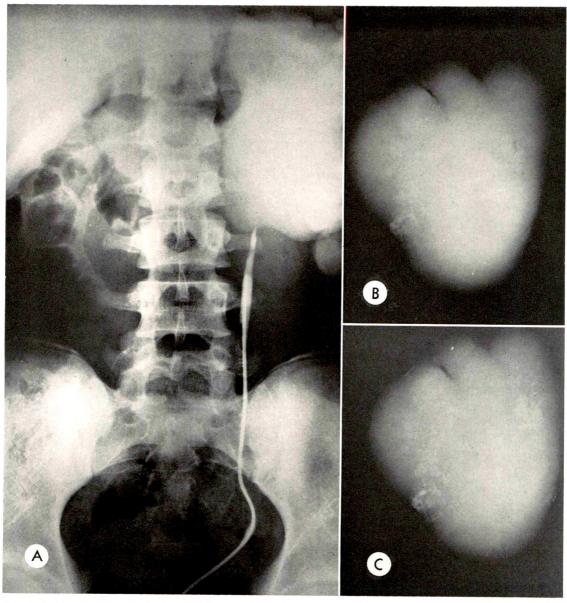


Fig. 1. A 16 year old male who has had intermittent abdominal pain since the age of 4 years. Left flank pain has been present since the age of 14 years at which time the diagnosis of pyelonephritis was first made. (A) Classic appearance of ureteropelvic obstruction. The exact junction of the ureter with the pelvis is not demonstrated. (B and C) Roentgenograms of the injected surgical specimen showing the ureter apparently having a high insertion in relation to the renal pelvis. The uppermost 3 cm. of the ureter was encased in and bound to the renal pelvis by a dense mass of calcification and fibrosis which microscopically showed chronic inflammation.

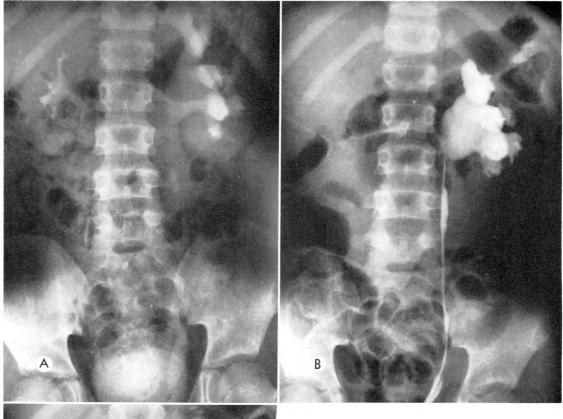




Fig. 2. A 7 year old male with known recurrent urinary tract infection for 2 years. (A) Intravenous pyelogram showing an appearance of the left renal pelvis which resembles that of traditional ureteropelvic obstruction. Note that the entire left ureter is dilated and tortuous with prompt visualization of the left kidney. (B) Retrograde pyelogram, done because of the intravenous pyelographic diagnosis of ureteropelvic obstruction, shows an appearance even more characteristic of this condition. (C) Cystogram with left vesicoureteral reflux shows the same appearance as B but the left ureter is again revealed to be dilated and tortuous. The renal pelvis filled easily by reflux and drained promptly without obstruction.

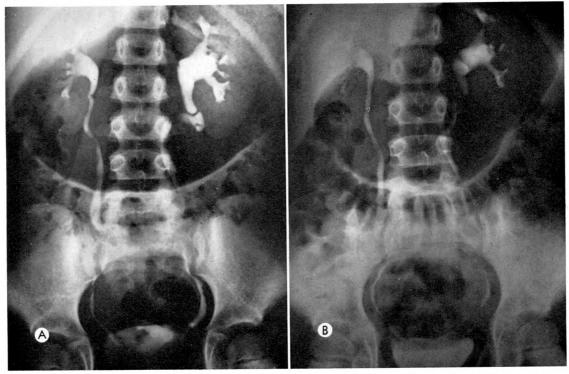


Fig. 3. Intravenous pyelogram of a 7 year old male with bilateral pyelonephritis. There was no reflux or obstruction demonstrated by cystography. (A) November 6, 1962. Each ureter is segmentally dilated and tortuous. The left ureter has a pronounced kink at the ureteropelvic junction which is the initial segment to kink. Minimal kinking is also present at the left ureterovesical area. (B) June 3, 1963. The segmental dilatation and tortuosity have improved after 7 months of antibiotic therapy. The kink at the left ureterovesical area has disappeared and the one at the ureteropelvic junction has decreased.

mobility and produces kinks at the site of junction of the mobile with the more fixed portions. The points of relative fixation in the ureter are at the ureteropelvic junction, bony pelvic inlet and ureterovesical junction—areas at which most ureteral obstructions are described.

The ureter kinks initially at the ureteropelvic junction during the early stages of dilatation and tortuosity (Fig. 3, A and B). Progressive dilatation, elongation, and tortuosity produce kinks at other sites, causing the ureter to fold upon itself by as much as 4 cm. (Fig. 4).

Infection and reflux, then, are responsible for the tortuosity and kinking which results in the roentgen appearance of ureteropelvic obstruction. The ureter below the apparent obstruction is dilated, tortuous and kinked in all instances but not all will show vesicoureteral reflux. In this

study, 23 of the 29 patients with nonobstructive renal pelvic dilatation simulating obstruction had reflux.

Hanley10 studied excretory pyelograms of 500 normal individuals and found that 90 per cent of the renal pelves were of the open type and that 10 per cent were of the closed type. After forcing fluids orally in patients with both types of pelves, he observed that the increased urine flow caused dilatation of the closed pelves but not of the open ones. This suggests that the closed type of renal pelvis is susceptible to earlier and more severe dilatation and may be the one which will most often show the appearance suggesting obstruction. In our material ureteropelvic obstruction was simulated in both types of pelves with the severity being related to the degree of ureteral dilatation, tortuosity and kinking rather than to the type of pelvis.

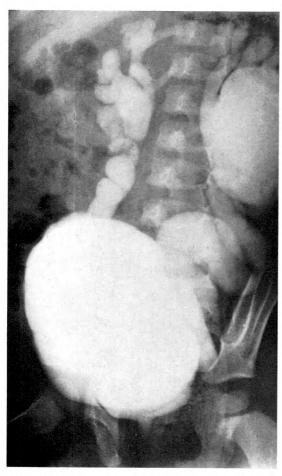


Fig. 4. Cystogram of a 6 year old female with vesicoureteral reflux revealing extreme dilatation, tortuosity, and kinking of each ureter. The wall of the ureter lies in an adjacent and parallel position and may become adherent. The usual sites of kinking are well demonstrated.

OBSTRUCTIVE DILATATION

The etiology of the pelvic dilatation in 6 patients with roentgenologically and surgically proven ureteropelvic obstruction was fibrotic bands in 4 and intrinsic stenosis in 2. The practice of utilizing intravenous pyelography and cystourethrography in the diagnostic work-up of children with urinary tract infection has resulted in a better understanding of the pathogenesis of this type of obstruction. Four of the 6 patients had previous examinations which showed no ureteropelvic obstruction but did show reflux and nonobstructive dilatation of the renal pelvis and ureter (Fig. 5, A, B and C).

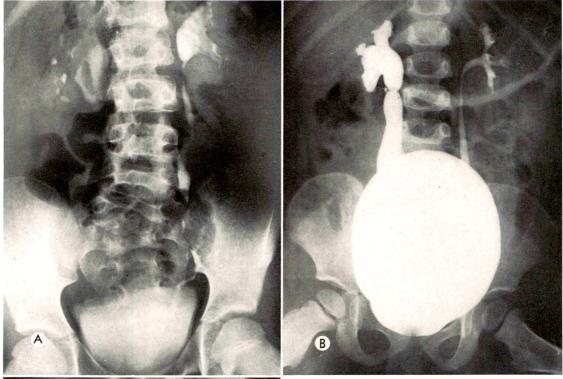
Another had a normal right kidney at the time that severe obstruction was demonstrated on the left only. Seven years later the patient developed obstruction in the previously normal right kidney (Fig. 6, A and B). This experience in these patients indicates that infection and reflux play a major role in the pathogenesis of ureteropelvic junction obstruction.

As explained earlier, infection and reflux cause pelvic and ureteral dilatation with secondary tortuosity and kinking of the ureter (Fig. 3, A and B). The ureteritis and periureteritis which accompany pyelone-phritis cause exudation, necrosis, stenosis and adhesions. The adhesions between the adjacent and parallel segments of the tortuous ureter, if severe enough, may produce secondary obstruction by compression or acute kinking. Stenosis due to mucosal and intramural inflammatory necrosis may occur at the sites of ureteral kinking, expecially at the ureteropelvic junction.

The findings in 4 patients who were operated on for nonobstructive dilatation which simulated obstruction confirm the role played by infection and reflux. All showed fibrotic thickening of the ureter and periureteral inflammatory adhesions, most marked at the sites of kinking (Fig. 7, A and B). The fact that the renal artery is sometimes found in relation to the stenosis and periureteral adhesions is purely an anatomic coincidence. It is easily encased within the periureteral inflammatory process because of its natural proximity to the ureter (Fig. 8, A and B).

The ureter was dilated, tortuous, and kinked below the obstruction in all 6 patients with adhesions and stenosis, as it was in those with nonobstructive dilatation. The 4 patients with adhesive ureteropelvic obstruction had fibrotic thickening of the ureter which was fixed in its bed by periureteral inflammatory tissue, as it was in those with nonobstructive dilatation due to infection and reflux.

One of the patients with ureteropelvic stenosis had previous intravenous pyelography and cystography that showed ureteral



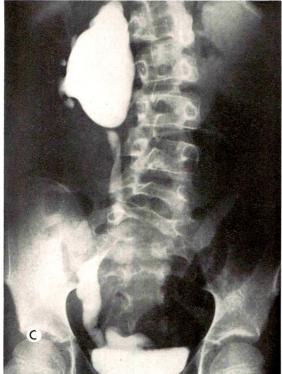


Fig. 5. A 5 year old female with a 4 year history of recurrent urinary tract infection. (A) Intravenous pyelogram at the age of 5 years. Poor excretion on the right due to ureteropelvic obstruction. The configuration of the left renal pelvis suggests the same diagnosis. Note that the left ureter below the narrowing is tortuous and dilated. Good drainage occurred from the left renal pelvis indicating nonobstructive dilatation at the present time. (B) Cystogram at the age of 3 years. Bilateral vesicoureteral reflux reveals marked dilatation of the entire right ureter with a narrowed kink at the ureteropelvic junction. No thought was given to organic obstruction at this time because there was no delay of right renal function in the intravenous pyelogram and there was drainage from the pelvis into the ureter. (C) Cystogram made at the same time as A and 2 years after B. Vesicoureteral reflux persists on the right and fills the renal pelvis above the stenosis which has occurred at the ureteropelvic junction. Organic obstruction was indicated by inadequate drainage, demonstrated in other parts of the examination. Operative findings confirmed the stenosis. The ureter was fibrotic, thickened,

dilated and fixed in its bed by periureteral inflammatory adhesions.

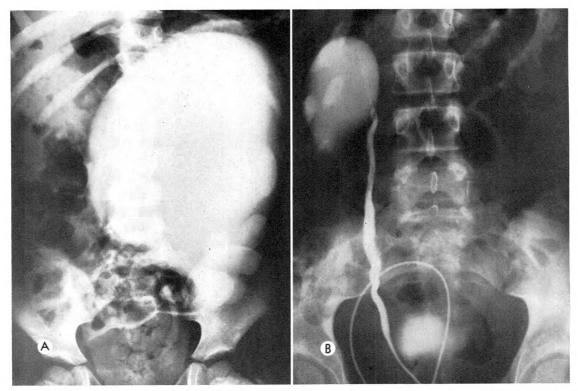


Fig. 6. A 5 year old female with a 3 year history of recurrent urinary tract infection. (A) May 17, 1957. Retrograde pyelogram demonstrating extreme and typical left ureteropelvic junction obstruction. The ureter is moderately dilated below the obstruction. The intravenous pyelogram at this time showed no function on the left and a normal kidney on the right. The ureter was bound to the pelvis by dense fibrous adhesions and was thickened and fibrotic. The adhesions had obstructed the ureteropelvic junction and microscopically there was chronic inflammation. (B) February 11, 1965. Retrograde pyelogram made 7 years and 9 months after A. There is typical right ureteropelvic junction obstruction due to inflammatory fibrotic adhesions binding the upper ureter to the pelvis. The ureter below the obstruction is dilated and was thickened by fibrosis.

dilatation and kinking due to infection and reflux (Fig. 5, A, B and C). The other had dilatation of the ureter below the stenosis shown in examinations subsequent to pyeloplasty (Fig. 9, A, B and C). Each patient with stenosis had fibrotic thickening and periureteral adhesions similar to those

TABLE I

CLASSIFICATION OF RENAL PELVIC DILATATION

- I. Non-obstructive Dilatation
 - A. Vesicoureteral Reflux
 - B. No Vesicoureteral Reflux
- II. Obstructive Dilatation
 - A. Secondary
 - 1. Vesicoureteral Reflux
 - 2. No Vesicoureteral Reflux
 - B. Primary

with nonobstructive dilatation and adhesive obstruction.

CLASSIFICATION OF RENAL PELVIC DILATATION

The conventional concept that renal pelvic dilatation and ureteropelvic kinking or narrowing are due to organic obstruction on a congenital basis is probably not valid. Nonobstructive dilatation and the role of infection and reflux in the pathogenesis of both nonobstructive and obstructive pelvic dilatation necessitate a new approach to this problem. A classification of the types of dilatation of the renal pelvis which takes into consideration the above mentioned factors is presented in Table I.

The division of the dilated renal pelvis

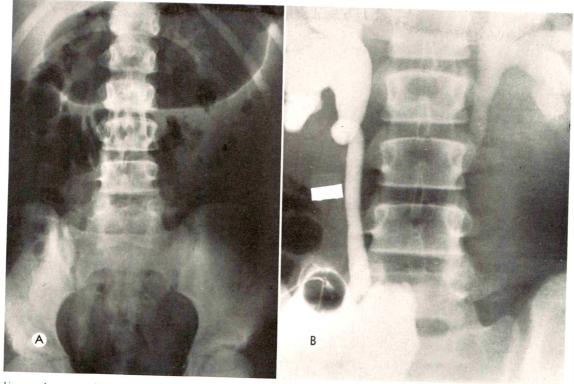


Fig. 7. A 4 year old female with known recurrent urinary tract infection for 3 years. (A) Intravenous pyelogram shows poorly excreting kidneys bilaterally. The only indication that there might be nonobstructive dilatation and reflux is segmental dilatation of the lower third of the right ureter. (B) The refluxing cystogram shows marked dilatation of the entire right ureter and kinking at the ureteropelvic junction. Drainage from the pelvis into the ureter was prompt. Fibrotic thickening of the ureter and periureteral adhesions, particularly at the site of kinking, were found at surgery.

into nonobstructive and obstructive types is made because the concept that dilatation does not always indicate obstruction is an unfamiliar one. Delayed renal excretion and poor pelvic drainage are established criteria of obstruction, but there has been a tendency to ignore their absence and consider all dilatation to be obstructive. Vesicoureteral reflux is another useful means of determining if dilatation is obstructive. There are many instances in which the presence of obstructive dilatation is equivocal in the excretory pyelogram and copious reflux on cystography fills the renal pelvis. Prompt drainage of the reflux filled pelvis indicates absence of obstruction.

The presence of reflux in nonobstructive pelvic dilatation has etiologic, therapeutic and prognostic significance. It has already been stated that reflux is one of the causes of nonobstructive dilatation. Failure to

demonstrate reflux on one occasion is not absolute evidence that it may not occur at other times. In either instance, however, the treatment should be medical and the response of the dilatation is more likely to be favorable if reflux is absent (Fig. 3, A and B). Reflux, if present, may respond to medical treatment, but, if not, a reflux correcting operation may be indicated.

That renal pelvic dilatation is caused by a secondary obstruction (Type II-A) is not an entirely new concept. There have been scattered reports of cases with inflammatory ureteral obstruction. 4.7.9 Vesicoure-teral reflux in this group has etiologic significance since its presence is a strong indication that the reflux and infection are the causes of the obstruction.

Reflux also has important therapeutic considerations in this group. Surgical attempts to correct the obstruction at the

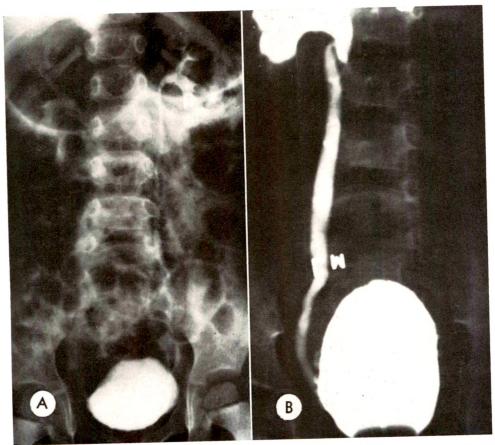


Fig. 8. A 3 year old male with a history of urinary tract infection for 1 year. (A) Intravenous pyelogram shows a relatively normal renal collecting system with no sign of obstruction. (B) Right ureteral dilatation and ureteropelvic kinking are revealed by the reflux in the cystogram. Pelvic drainage was adequate. Periureteral adhesions at the kinked ureteropelvic junction were found at operation. The renal artery was encased in the adhesions but neither caused obstruction.

ureteropelvic junction probably will fail if reflux is present and uncorrected because the pathogenetic situation remains unchanged. If reflux is absent, a dilated, tortuous ureter below the obstruction signifies that infection and reflux have been previously present and the ureteral dilatation is an irreversible residual. Surgical relief of the ureteropelvic obstruction would again only recreate the pathogenetic situation, *i.e.*, an open ureteropelvic junction with a dilated and tortuous lower ureter.

The results of surgical attempts to correct this type of obstruction have been poor. It is felt that the dilated ureter below the obstructive point, with or without reflux, is the major factor responsible for the disappointing results. Treatment should

be directed toward the existing infection and the generalized ureteral dilatation, which may be refluxing, before attention is given to the secondary ureteropelvic obstruction. It may not always be possible to completely eradicate infection by medical management alone. Several investigators^{1,2,3,12,20} have designed operations by which to correct reflux and reconstruct the dilated ureter, and thus assist in eradicating refractory infection. This approach to secondary, obstructive dilatation of the renal pelvis will also guard against areas of existing stenosis and kinks in the lower ureter and should improve the surgical results.

Primary obstructive renal pelvic dilatation (Type II-B) has proven to be ex-

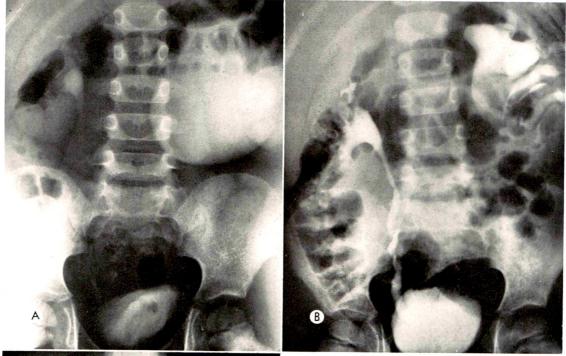




Fig. 9. A 5 year old male with a 5 month history of left flank pain associated with urinary tract infection. (A) December 7, 1964. Left ureteropelvic junction obstruction shown on excretory pyelogram. Function of the left kidney was delayed and no drainage occurred from the pelvis. There was no vesicoureteral reflux on either side. Operative findings were stenosis of a 2 cm. segment of ureter which was bound in its bed by inflammatory adhesions. Microscopically there was chronic inflammatory disease. (B) January 15, 1965. Excretory pyelogram after left pyeloureteroplasty and nephrostomy drainage. The left ureter could not be filled by this examination or by reflux. (C) April 22, 1965. The left renal pelvis remains dilated in the excretory pyelogram and the left ureter is seen to be dilated and tortuous. Note the dilatation and tortuosity of the right ureter in B and C, which may indicate that it is a candidate for pathology similar to that on the left.

tremely rare when the whole problem is considered in view of the concepts and proposed classification presented in this paper. It should be regarded as being congenital, whether due to stenosis, band or vessel. The criteria for this type of obstruc-

tion are that it occurs at a relatively early age, is quite severe, and the ureter below is small from disuse (Fig. 10). It is possible that this group will fall into the familiar category of the cystic dysplasias of the kidney, *i.e.*, cystic hydronephrotic, cystic

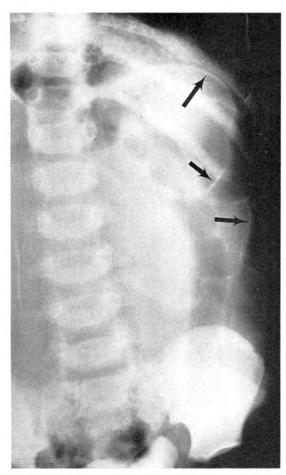


Fig. 10. A 15 month old male who presented with a left flank mass. Intravenous pyelogram shows delayed excretion and crescents (arrows), which are usually due to opacified renal parenchyma compressed by dilated calyces. Severe stenosis of the ureteropelvic junction and cystic hydronephrosis were found at operation. The ureteral body was hypoplastic, indicating disuse.

hypoplastic and multicystic kidneys. Ureteral stenosis and atresia are commonly but not invariably found with these conditions and the relationship of the two is not clear at the present time. The presence of dysplastic renal elements, in association with ureteropelvic obstruction, is thought to be evidence in favor of the primary type because it indicates interference with the development of the fetal or neonatal kidney. These cases are not completely understood and it is anticipated that additional information will be forthcoming to provide clarification.

DISCUSSION

Gondos⁷ has stated that organic ureteral stenosis and adherent kinks are most commonly the result of chronic pyelonephritis and should be considered an indication of such unless proven otherwise. He specifically excludes the ureteropelvic and ureterovesical areas. However, he reports 2 cases of stenosis and adherent kink of the body of the ureter in which there was also narrowing of the ureteropelvic junction that was considered congenital.

The relationship of the pathogenesis of nonobstructive to secondary obstructive dilatation of the renal pelvis indicates that Gondos' concept should be extended to include obstruction at the ureteropelvic junction. Ureteral dilatation below the obstructive point and the presence of vesicoureteral reflux in a given patient are specific signs that the obstruction is acquired and secondary to infection and its ravages; *i.e.*, reflux, dilatation, tortuosity, kinking, periureteral fibrosis and intrinsic stenosis. It seems likely that these same principles apply to the ureterovesical obstruction.

SUMMARY

- 1. Thirty-five patients with renal pelvic dilatation resembling ureteropelvic junction obstruction have been studied to determine the pathogenesis.
- 2. Twenty-nine of the patients had nonobstructive and 6 had obstructive dilatation.
- 3. A classification of the types of renal pelvic dilatation is presented which has etiologic, therapeutic and prognostic signicance.
- 4. The nonobstructive variety is a manifestation of generalized renal collecting system dilatation in which the pelvis, if considered alone, exhibits features typical of ureteropelvic junction obstruction.
- 5. Ureteral dilatation, tortuosity and kinking with extrinsic and intrinsic fibrosis due to infection and reflux are the pathogenetic factors involved.
- 6. Roentgen and surgical findings indicate that the pathogenesis is the same in

the nonobstructive and secondary obstructive types of renal pelvic dilatation.

7. Primary obstructive ureteropelvic dilatation is rare and it is believed that renal pelvic dilatation is not always obstructive or congenital.

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OBSTRUCTION OF THE LOWER URETER BY THE DISTAL HYPOGASTRIC (UMBILICAL) ARTERY*

By RICHARD T. TRACKLER, M.D., and WILLIAM H. McALISTER, M.D. ST. LOUIS, MISSOURI

VASCULAR obstruction of the lower ureter was first emphasized by Hyams⁷ in 1929. Since that time there have been several reports in the urologic literature.^{1,2,4,6,10} We wish to report a case of a male infant with obstruction of the lower third of the ureter due to an obliterated distal hypogastric (umbilical) artery.

REPORT OF A CASE

D.L., a 20 day old male infant, was admitted to the St. Louis Children's Hospital for evaluation of a Ladd and Gross Type III imperforate anus for which he had a sigmoid colostomy performed I day after birth. The patient had a normal birth weight and was the product of a normal pregnancy and delivery.

Routine laboratory data including urinalysis were normal. Intravenous urography was performed because of the urinary tract abnormalities known to be associated with imperforate anus. A partially obstructed distal left ureter was demonstrated (Fig. 1, \mathcal{A} and \mathcal{B}). Cystography and distal colostomy injection showed a rectourethral fistula. The spine was roentgenographically normal.

The patient had an exploratory laparotomy at 2 months of age. An enlarged, obliterated distal hypogastric (umbilical) artery was found lying anterior to and obstructing the distal left ureter. A segment of the offending vessel in the area of the ureter was removed and the obstruction was relieved.

A follow-up intravenous urogram made I year later demonstrated decreased ureteropyelocaliectasis on the left side (Fig. 2). The patient had no signs or symptoms of urinary tract infection. A successful Swenson's rectal pull-through procedure and closure of the rectourethral fistula have been accomplished.

DISCUSSION

The hypogastric or internal iliac artery is a direct continuation of the common iliac

artery. In the fetus, it ascends from the pelvis along the side of the bladder to and along the back of the anterior abdominal wall. It joins its counterpart on the other side at the umbilicus. After passing through the umbilical opening, the hypogastric arteries are continued as the umbilical arteries in the umbilical cord to the placenta. Other authors 7,9,10 identify the distal portion of the hypogastric artery extending from the pelvis to the umbilicus as the umbilical artery.

Following the cessation of blood flow through the umbilical artery, the function of the distal end of the hypogastric artery is suspended. This portion of the vessel undergoes rapid atrophy and obliteration. It is converted into a solid, fibrous cord referred to as the lateral umbilical ligament or obliterated hypogastric artery, which extends from the pelvis to the umbilicus.³

Based on a study of 20 male cadavers, Hyams⁷ described the pelvic blood vessels and their close association with the ureters. He stressed the wide variation both in the course and in the distribution of these vessels. The vessels obstructing the ureter were from the anterior division of the hypogastric artery. They were usually the umbilical artery (or distal hypogastric artery as described above) or the inferior vesical arteries. Variation in the normal course of either the ureter or the vessels could result in ureteral compression. The obstructing vessel could be artery or vein or both and could have an associated fibrous band. The vessels were either patent or obliterated. The actual site of obstruction might be anywhere in the distal ureter, but was usually located from the bony pelvic inlet to just above the ureterovesical junction.

The case of distal ureteral obstruction

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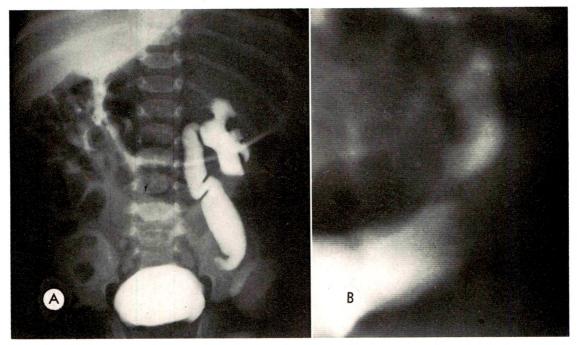


Fig. 1. (A) Intravenous urogram at 1 month of age showing partial obstruction of the distal left ureter. (B) Fluoroscopic spot roentgenogram of the distal left ureter demonstrating a transverse filling defect above the ureterovesical junction.

described by Hyams⁷ was that of an adult male with the distal left ureter crossed by an artery and fibrous band 6 to 7 cm. above the ureterovesical junction. Campbell¹ reported a 13 month old girl with a left ureterovesical stricture and secondary vascular compression of the distal ureter. Greene et al.⁶ reported 2 adult males with patent aberrant vessels obstructing the distal left ureters. The ureters appeared intrinsically normal after ligation and resection of only the vessels.

Young and Kiser¹⁰ reported 5 male patients, 3 children and 2 adults, with distal ureteral obstruction secondary to pelvic vessels. The offending vessel was thought to be the umbilical artery (distal hypogastric artery) in 3 patients and was not absolutely identified in the remaining 2 patients. Two of the 5 patients had resection of the involved portion of the ureter with subsequent uretero-neocystostomy because of persistent constriction of the ureter after resection of the vessels. In the few cases of distal ureteral obstruction secondary to

pelvic vessels thus far reported, the obstruction was found more commonly in males and on the left side.

The urographic demonstration of a transverse filling defect of the distal ureter above the ureterovesical junction with some visualization of the ureter distal to the defect is the roentgenographic finding of greatest suggestive diagnostic value for ureteral obstruction secondary to pelvic blood vessels (Fig. 1B).

Other possibilities in the differential diagnosis of a transverse filling defect of the distal ureter would include kinks or ureteral valve-like folds. Kinks in the ureter usually develop above an obstruction. Dilatation of the ureter distal to a kink would exclude obstruction secondary to pelvic vessels. Ureteral valve-like folds are not uncommon in the upper ureter. They may persist in adults as subepithelial buds. These folds are rarely associated with obstruction.

Congenital stricture is demonstrated most commonly in the upper third of the ureter. The ureteral meatus, intramural



Fig. 2. Intravenous urogram at 14 months of age showing decreased uretero-pyelocaliectasis. The distal sigmoid colon and rectum are filled with contrast material from earlier demonstration of the recto-urethral fistula.

portion of the ureter or both are the next most commonly reported sites of congenital ureteral stricture.⁴ Strictures associated with chronic inflammatory processes such as tuberculosis will have evidence of disease in the kidney and other portions of the ureter. An isolated stricture of the ureter occurring without surgical procedures may be differentiated by the tapering edges of the defect.

Retroperitoneal fibrosis affects a greater portion of the ureter. It is usually bilateral and rarely involves the ureter below the pelvic inlet. The ureters are characteristically displaced medially in this condition.

The clinical history and the lack of a sharply defined, transverse filling defect in the ureter will aid in the diagnostic exclusion of strictures secondary to ureteral calculus removal, pelvic malignancy or inflammatory disease, primary ureteral tumors, nonopaque calculi, blood clots, endometriosis affecting the ureter, adhesions

secondary to surgery and partial ureteral ligation from surgical procedures in the pelvis including inguinal hernia repair.

SUMMARY

A case of an obliterated, distal hypogastric (umbilical) artery partially obstructing the lower left ureter of a male infant is reported. Surgical resection of the offending vessel resulted in decreased uretero-pyelocaliectasis. The urographic demonstration of a transverse filling defect of the distal ureter above the ureterovesical junction with some visualization of the ureter distal to the defect is the most valuable roent-genographic finding for ureteral obstruction secondary to pelvic blood vessels. The previously reported cases are reviewed and the differential diagnosis is discussed.

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THE EFFECT OF ACUTE AND CHRONIC URETERAL OCCLUSION UPON RENAL HANDLING OF Hg²⁰³ CHLORMERODRIN

By GERALD S. JOHNSTON,* and GERALD P. MURPHY†

BSTRUCTION of the ureter, either partial or complete, may result following trauma; during pregnancy; as a consequence of renal stone, of infection, of bleeding and of tumor growth; or incidental to ureteral obstruction. Corrective surgery can frequently prevent the loss of renal function. However, evaluation of remaining renal function can be difficult in the presence of ureteral obstruction. Questions arise concerning the probable duration and degree of obstruction, the advisability of immediate intervention versus a more conservative approach to the problem, and the probability of recovery of renal function after surgery for correction of the obstruction. We performed the following study in an attempt to find the place of the Hg²⁰³ chlormerodrin renal scintiscan in answering these questions.

MATERIAL AND METHOD

Fifty-seven experiments were performed on adult male and female mongrel dogs* with a body weight range from 9.5 to 14.6 kg. Animals were anesthetized with intravenous pentobarbital, 30 mg./kg., for the duration of the experimental periods. During measurement of renal blood flow, animals were adequately heparinized (2.5-4.0 mg./kg., intravenously) and were assisted in respiration of room air by means of a Harvard respirator attached to a cuffed, endotracheal tube. An intravenous solution of half-normal saline and 5 per cent dextrose was administered into the right jugular vein at rates of 3.7 to 6.0 ml./min. during all observation periods.

Renal blood flow was measured directly (DRBF) by a method which employed cannulation of the renal vein and the use of a calibrated Sigmamotor pump. This method has been previously described elsewhere in detail.5 Mean aortic blood pressure, renal venous pressure (RVP) and ureteral pressure (UP) were measured and recorded. Renal resistance (RR) was calculated by dividing the flow (DRBF) in ml. /min./gm. of kidney into the blood pressure in mm. of Hg lost across the kidney (mean aortic pressure minus the renal venous pressure). At the completion of each experiment, kidneys were weighed to the nearest 0.1 gm. Acute unilateral occlusions were simulated by the occlusion of a ureteral catheter. Prolonged unilateral ureteral occlusions were surgically produced by double-ligation and transection of the ureter at the level of the iliac vessels or at the ureteropelvic juncture (high ligation). Partial ureteral occlusions were produced with silk sutures at the level of the iliac vessels. All animals received penicillin, 600,000 units intramuscularly, for 3 days postoperatively.

The following 8 time periods and 22 experimental subgroups were employed (Fig. 1).

Period I—Acute ureteral occlusion, with subgroups: (A) released; (B) not released; (C) not released (pre-treated with epinephrine 2.8-7.6 µg./min. intravenously to induce renal vasodilatation); (D) released, high ligation; and (E) released 2 days post right nephrectomy.

Period II—One day ureteral occlusion, with subgroups: (A) right released; and (B) left released.

Period III—Two day ureteral occlusion,

^{*} The principles of laboratory animal care as promulgated by the Society for Medical Research were observed.

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PERIOD	URETERAL OCCLUSION TIME	SUB-GROUP	PRE-TREATMENT		RENAL RADIOACTIVITY LEFT RIGHT				RENAL SCINTISCAN	
				CORTEX	MEDULLA		MEDULLA	LEFT	RIGHT	
I		A RELEASED		99,523	14,612	98,865	13,701	•	*	
		B.NOT RELEASED	,	23,602	5,134	26,098	4,829			
		C.NOT RELEASED	EPINEPHRINE 5 בע min L.V.	53,471	13,251	50,967	6,512		*	
		D HIGH LIGATION, RELEASED		48,037	3,559	46,204	4,412		*	
		E. RELEASED	NEPHRECTOMY, RIGHT 2 DAYS PRIOR	60,838	4,412	_				
П	ONE DAY	A RELEASED, RIGHT		80,595	7,628	34,188	5, 484	*	4.	
		B RELEASED LEFT		52,865	5,485	78,545	5,557	*	3	
Ш	TWO DAYS	A RELEASED		71,154	24,813	115,365	38,672		9	
		B NOT RELEASED		53,561	8,972	103,936	12,218	4	•	
ΙV	THREE DAYS	A.RELEASED		80,653	12,655	127,333	16,252	6	9	
		B. NOT RELEASED		22,771	10,591	151,338	13,718	,	9	
		C RELEASED AND STUDIED I WEEK LATER		72,634	9,140	90,000	10,480	蒙	9	
∇	FOUR DAYS	HIGH LIGATION RELEASED		127, 040	14,162	258,237	43,745	6	9	
VI	ONE WEEK	A RELEASED		10,885	3,789	19,594	5,267			
		B. NOT RELEASED		19,594	11,400	89,340	5,535		9	
		C RELEASED	PHENOXYBENZAMIN	E 16,992	6,435	192,243	13,263		9	
VII	TWO WEEK!	A.RELEASED		6,235	7,155	65, 743	9,385	3		
		S B. NOT RELEASED		2,833	2,329	98,042	4,703		-	
		C. RELEASED	PHENOXYBENZAMIN	24,63°	7 12, 176	226,116	21,796		•	
ΔΠ	FIVE WEEK	1		5,115	2,086	51,019	5,124		1	
		B. NOT RELEASED		13,05	0 3,574	123,050	6,958		9	
		C RELEASED	PHENOXYBENZAMI	NE 5,595	2,951	69,50	9 6,378		9	

Fig. 1. One sample from each of the experimental subgroups is shown. The left ureter was occluded in every example except 1 in Period 11, subgroup A, where the right ureter was occluded. Pre-treatment with epinephrine, phenoxybenzamine or contralateral nephrectomy had little effect on the primarily time related impairment of renal function following complete ureteral occlusion.

with subgroups: (A) released; and (B) not released.

Period IV—Three day ureteral occlusion, with subgroups: (A) released; (B) not released, and (C) released and studied I week later.

Period v—Four day ureteral occlusion, high ligation.

Period vi—One week ureteral occlusion, with subgroups: (A) released; (B) not released; and (C) released, pretreated with phenoxybenzamine.

Period VII—Two week ureteral occlusion, with subgroups: (A) released; (B) not released; and (C) released, pretreated with phenoxybenzamine.

Period VIII—Five week ureteral occlusion, with subgroups: (A) released; (B) not released; and (C) released, pretreated with phenoxybenzamine.

Thirty microcuries of Hg208 chlormerodrin were given intravenously at the time of, or 45 minutes prior to study or to release of obstruction. In both groups of ureteral occlusions (acute or chronic), some occlusions were released prior to study while others were not. Timed and accurately measured urine samples were collected, when available, for radioisotope assay. Formalin-fixed renal tissues (cortex and medulla) were analyzed for radioactivity (counts per minute per gram of tissue) using a sodium iodide crystal well-counter. Scintiscans were obtained of the excised organs. Renal tissues were mounted and stained with hematoxylin and eosin and studied with the aid of light microscopy. A system of double blind quantitation of the degree of morphologic damage (o to 4+) was attempted.

RESULTS RENAL HEMODYNAMICS

Acute ureteral occlusion was generally characterized by an average increase in direct renal blood flow (DRBF) of 29 per cent and a rise in renal venous pressure (RVP) of 5.4 mm. Hg with little change in mean aortic blood pressure (10 mm. Hg). During this time, renal resistance (RR) fell 32.5

per cent, average. Ureteral urine pressures during acute occlusions in the present experimental conditions averaged 38.1 mm. Hg (range 14.8 to 67 mm. Hg). After the release of acute ureteral occlusions DRBF and RVP fell and RR rose. Phenoxybenzamine (dibenzyline) pretreatment⁴ diminished all the preceding acute responses. However, epinephrine infusion, contralateral nephrectomy, partial ureteral occlusion or variation of the level of ureteral occlusion did not affect the hemodynamic response.

Prolonged ureteral occlusions, from I through 4 days, were all associated with low renal blood flows and high RR, at similar levels of ureteral pressure. Upon release of the chronic ureteral occlusion, renal blood flow and renal venous pressure rose, and renal resistance fell. This response, even at 5 weeks, could be diminished by prior phenoxybenzamine (dibenzyline) treatment. Thus, a state of renal vasodilatation characterized both the response to acute ureteral occlusion and the response to the release of chronic ureteral occlusion.

RADIOMERCURY CHLORMERODRIN DYNAMICS

When the ureter was experimentally occluded (Fig. 1), proximal tubular function was presented with an increasing intraluminal pressure. Initially, this pressure was partially dissipated as it distended the renal pelvis. Scintiscans and measurement of tissue content of radioactivity reflected little or no change in renal function during and following acute occlusion. After 24 hours of unilateral occlusion, a difference between the two kidneys was readily seen on the scintiscans and in the measured concentration of radioactivity in the kidney tissue. With each additional day of occlusion, this difference increased. As the renal pelvis dilated and compression of renal parenchyma occurred, the pelvis could be seen on the scan (Fig. 1).

Releasing the ureteral occlusion prior to study permitted more accumulation of radiomercury in the kidney than did maintaining the occlusion throughout the study period. A week of recovery time following 3 days of occlusion allowed for increasing improvement of function, but not complete recovery. Following I week of occlusion, very little function could be detected in the kidney with the occluded ureter. After from 2 to 5 weeks of occlusion, renal tissue radiomercury concentration was reduced approximately 10 per cent of that of the unoccluded kidney and very little variation occurred after the second week in radiomercury distribution. With reduction in function of the kidney with the occluded ureter, there was an increase in isotope concentration in the contralateral unoccluded kidney. This would appear to be a consequence of the availability of more Hg²⁰⁸ for excretion by the normal kidney. Figure

2 shows a typical response to an acute ureteral occlusion. There was little or no detectable effect on the urinary concentration or excretion of Hg208 chlormerodrin. Figure 3 shows the characteristic response to the release of a 4 day ureteral occlusion. By this time period, a significant reduction in the urinary Hg203 excretion could be detected. In Figure 4 the low fixed urinary concentration of Hg²⁰³ is shown in an animal following the release of a 5 week ureteral occlusion. Neither epinephrine pretreatments (vasoconstriction) nor dibenzyline pretreatment (vasodilatation) had any detectable effect upon the renal dynamics of Hg208 chlormerodrin in any of the acute or chronic experimental subgroups. The progressive reduction in the urine levels of

URETERAL OCCLUSION (ACUTE)

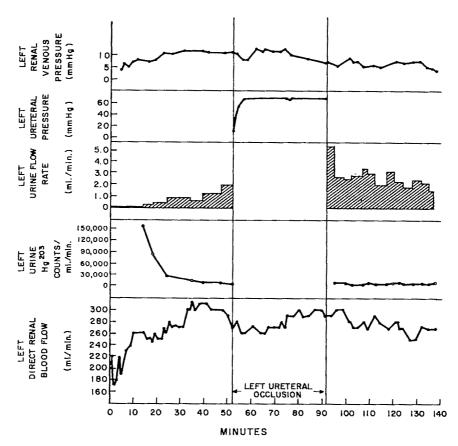


Fig. 2. The left ureter was occluded for approximately 40 minutes in this experiment. This did not demonstrably change the renal venous pressure, the urine flow rate, the Hg²⁰³ concentration in the urine or the directly measured renal blood flow.

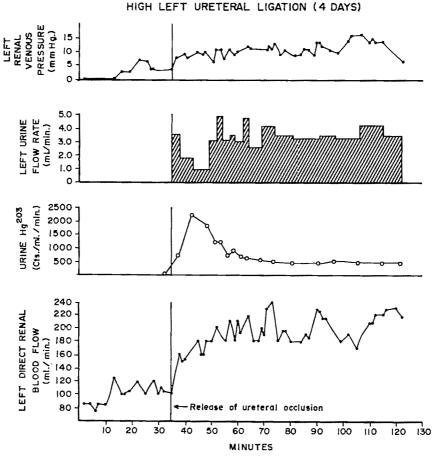


Fig. 3. Following 4 days of left ureteral occlusion, the ligature was removed from the left ureter. Urine flow was promptly re-established and renal blood flow improved. Urine Hg²⁰³ excretion, however, was much lower than normal.

Hg²⁰³ chlormerodrin correlated best with the duration of the ureteral occlusion. Thus, in the presence of ureteral obstruction, variations in renal blood flow, the level of ureteral occlusion, and the presence or absence of the contralateral kidney had no detected effect upon the renal excretion of Hg²⁰³ chlormerodrin. Animals studied I week after the release of a 3 day ureteral occlusion continued to demonstrate significant reduction in the excretion rate of Hg²⁰³ chlormerodrin.

RENAL HISTOPATHOLOGY

Serial examination by light microscopy of hematoxylin and eosin stained kidney tissue slides from the acute and chronic ureteral occlusion subgroups supports and extends the results obtained with scintiscanning and radiomercury tissue assay. These results quantitated on a o to 4+ basis were studied without knowledge of the origin of the tissue being examined. No abnormal microscopic changes in glomerular, interstitial or tubular structure were detected in acute ureteral occlusion states, at low or high ureteral levels, in the presence or absence of a contralateral kidney, with vasoconstrictors or vasodilators, or with partial or complete occlusion. Acute or chronic inflammatory responses were not present, and tubular dilatation was minimal (0 to 1+). Progressive tubular dilatation was, however, noted at 1, 2, and 3 day occlusions (Fig. 5, A-F). Tubular dilatation to the point of rupture with urinary extra-

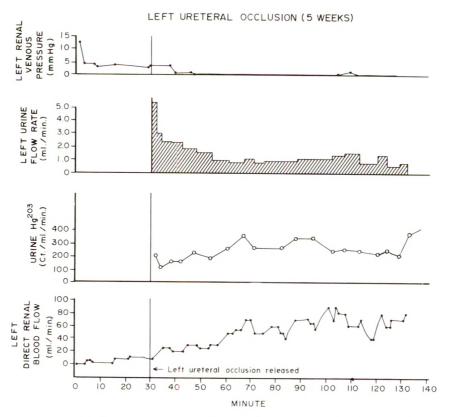


Fig. 4. Measurements made following the release of a 5 week ureteral occlusion showed a low urine flow rate with a low, fixed Hg²⁰³ concentration. Renal blood flow improved after the removal of the intrapelvic pressure.

vasation was first detected after 4 days of high ureteral occlusions (Fig. 5A). Vacuolization of the tubular cytoplasm (Fig. 5B), peritubular hemorrhage (Fig. 5C), and deposition of intraluminal tubular proteinaceous casts was also first noted after the 1 day occlusion (Fig. 5D). These alterations were progressive to a maximal point of 4 days ureteral occlusion. Little inflammatory response was noted (1+ to 2+), and no detectable glomerular fibrosis, or necrosis was concomitantly observed.

Periglomerular fibrosis and intraglomerular fibrosis (Fig. 5E) were prominent and progressive from 1 to 5 weeks after ureteral occlusion (1+ to 3+). Concomitant interstitial scarring and fibrosis were also progressively evident. Inflammatory responses, both acute and chronic, were encountered over this period (Fig. 5F). Tubular collapse rather than dilatation was evi-

dent during the I to 5 week ureteral occlusions. Kidneys examined I week after the release of the 3 day ureteral occlusion demonstrated similar morphologic changes in the interstitial and glomerular structures. Progressive pelvic dilatations were present on direct examination and noted on the scintiscans. Renal parenchymal atrophy and compression were seen in association with the progressive hydroureter-nephrosis. Thus, the major and significant morphologic changes were observed in the renal tubular cells. The grossly noted development of renal capsular and ureteral collateral vessels had no apparent effect on the observed renal morphologic changes.

DISCUSSION

Radiomercury chlormerodrin has been used in performing radioisotopic renal function evaluations since 1960. The dosage

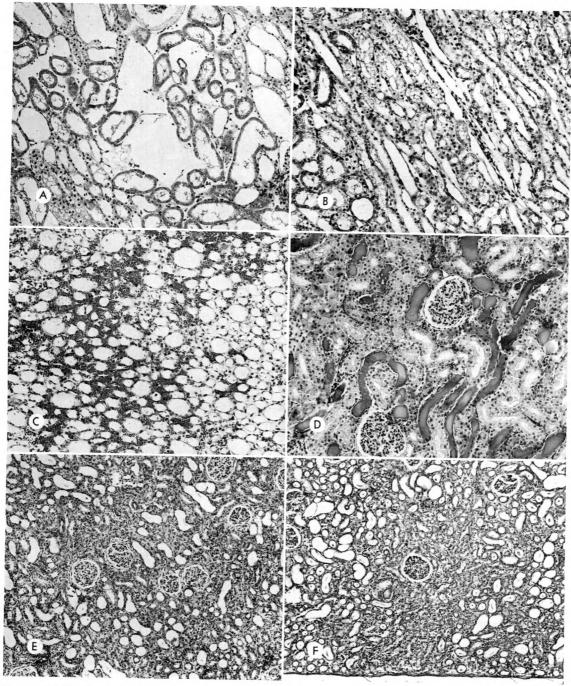


Fig. 5. (A-F) Renal photomicrographs of changes in histology following ureteral occlusion. (A) Tubular dilatation; (B) vacuolization of tubular cytoplasm; and (C) peritubular hemorrhage is present after 4 days. (D) Intratubular proteinaceous casts were present after 1 day of occlusion. (E) Periglomerular and intraglomerular fibrosis is seen following 1 week to 5 weeks of occlusion. (E) Changes of inflammation are also present over the 1 to 5 week occlusion period $(H \& E \times 150)$.

of chlormerodrin in these instances is far below that necessary to induce diuresis. Various studies have demonstrated the usefulness of this radioisotopically tagged agent in scintiscanning³ and in renography. Radiomercury chlormerodrin renograms and scintiscans provide information about the blood supply to the kidney. In addition, chlormerodrin appears to be secreted by the proximal convoluted tubule. Since the function of the proximal tubule cells is reflected in these radioisotopic tests, a process which interferes with the circulation to and/or the functioning of the proximal tubular cells will result in impairment of the manner in which chlormerodrin is usually removed from the circulating blood by the kidney. The renal dynamics of chlormerodrin, therefore, reflect the functioning renal tubular mass. In addition, the renal ability to transport the radioactive mercury in chlormerodrin from the circulating blood to the excreted urine reflects the adequacy of the renal circulation, particularly as compared to the contralateral kidnev.2

In the present study, states of prolonged ureteral occlusion were characterized by a progressive decline in renal cortical concentration of Hg²⁰³ (the only portion of the radiomercury chlormerodrin molecule detected by the methods employed). The possible mechanisms which might interfere with the orderly excretion of this diuretic substance appear to be both the degree to which glomerular filtration pressure buildup may impair the function of renal proximal tubule cells, and the extent to which this same pressure and the renal calveeal deformities may cause inadequacy of the renal circulation (Fig. 1). As with other bodily functions, impairment of circulation would most likely result in the most likely disturbance, but these features are obviously not differentiated by the renal scintiscans.

The mechanism of decrease in Hg²⁰³ concentration in the kidney with ureteral occlusion may give some clues concerning the mechanism of kidney damage in this state. When the ureter is occluded, pressure

from the filtering glomeruli is transferred to the kidney tissues adjacent to the renal pelvis. As this tissue pressure increases, distention into the kidney can be seen on the scan of the excised kidney (Fig. 1) and upon direct examination. The pressure transmitted to the renal tissues, as shown by the rising renal venous pressures, soon becomes high enough to significantly occlude renal blood flow. Apparently, renal blood supply is decreased both directly, in some renal areas, and also indirectly by means of the reflex changes in renal autoregulatory tone.

Renal parenchymal damage results and soon there follows an apparently irreversible (within the time periods employed here) state of decreased renal function. The collateral vessels seen in the renal capsule and ureter appeared to provide no functional benefit. Ureteral occlusion must be relieved as early as possible since the resultant renal parenchymal damage is progressive following ureteral obstruction. Although kidney function appears to return if urinary drainage is re-established within 3 days, prompt return of function was not observed after 4 days of ureteral occlusion in these studies. This 4 day experimental effect has also been noted by Simmons et al.7

Renal scintiscanning with radiomercury chlormerodrin as the agent is capable of affording much information about the degree, the site (right, left, or bilateral) and duration of ureteral occlusion. This technique should be freely utilized to aid in the evaluation of patients with urinary obstruction.

CONCLUSIONS

- 1. The principal detectable effects of ureteral occlusion on the renal scintiscan as determined in this study are a progressive reduction in proximal tubular Hg²⁰³ chlormerodrin concentration and a diminution in renal blood flow.
- 2. A normal appearing Hg²⁰³ chlormerodrin renal scan was obtained following acute ureteral obstruction of up to 60 minutes' duration.
 - 3. A I day ureteral occlusion signifi-

cantly reduced the isotope concentration in the affected kidney, but continuing renal function could be detected.

- 4. Following 2 days of ureteral occlusion, further diminution in isotope concentration was seen in the ureterally occluded kidney. A dilated renal pelvis was detectable on scintiscan. Release of the obstruction resulted in prompt improvement in isotope concentration.
- 5. After 3 days of ureteral occlusion, prompt restoration of renal functions occurred when urinary drainage was re-established. Beyond the fourth day of ureteral occlusion, the prompt restoration of renal functional capacity was not observed.
- 6. The renal handling of Hg³⁰³ chlormerodrin during and following the release of ureteral occlusion proved to be an early and an accurate indication of the degree to which prompt renal tubular and vascular recovery could be expected following the re-establishment of urinary drainage from the ureterally occluded kidney.

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NONOBSTRUCTIVE HYDRONEPHROSIS AND HYDROURETER*

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THE concept that dilatation of the renal collecting system always indicates obstruction is deeply ingrained in medical thought and teaching. It has persisted in spite of the fact that dilatation without obstruction occurs in tubular structures elsewhere in the body, e.g., in the aorta with hypertension, in the bowel with ileus, and in arteries and veins with increased blood flow. The absence of a proven point of obstruction in many instances of hydronephrosis and hydroureter has not prevented propagation of the belief that the dilatation must be due to organic obstruction.

The first clue that hydronephrosis and hydroureter are not invariably related to organic obstruction has been provided by cystourethrography. Considerable dilatation of the ureter, pelvis and calyces is commonly demonstrated by reflux on the cystogram where little or none is seen in the intravenous pyelogram (Fig. 1, A and B). Obstruction remained as part of the pathogenesis, however, because infravesical obstruction seemed to be a logical explanation in the earlier concepts of reflux. Numerous studies of the etiology of reflux now reveal that it is not necessarily secondary to obstruction, but, on the contrary, is often present without obstruction. 3, 6, 7, 10

The purpose of the author is to report the results of a clinical study of patients exhibiting nonobstructive dilatation of the urinary tract and discuss possible etiologic mechanisms.

MATERIAL AND METHODS

One hundred and twenty patients with acute urinary tract infection were examined by intravenous pyelography, cystoure-thrography, and fluoroscopic study of the

calyces, pelves and ureters when filled by contrast material during intravenous pyelography. The patients were selected from a total group of over 350 with urinary tract infection according to the following criteria: (1) absence of obstruction, (2) presence of acute infection and (3) absence of any type of neurologic deficit.

Intravenous pyelography consisted of exposures in the anteroposterior, both oblique, and posteroanterior positions 3 to 10 minutes after the injection of the opaque material. No ureteral compression was used to avoid any possibility of it producing dilatation.

Cystourethrographies were performed under fluoroscopic control and roentgenography of the bladder and urethra was done with a conventional photo-timed spot film device according to a method previously described.¹⁶

Fluoroscopy of the renal collecting conduits was performed by conventional fluoroscopy in 28 patients, by image amplification and mirror viewing in 35, and by television viewing in 63. Cinefilming was done in 15 patients but was discontinued since little information was gained beyond that obtained by fluoroscopy and the radiation dosage was much higher.

ILEUS AND ATONY

Ninety-three of the 120 patients had evidence of ileus and atony. The requirements for establishing the presence of ileus were segmental or generalized dilatation, persistent filling, poor peristalsis, and reversed peristalsis.

The lower spindle of the ureter most often showed segmental dilatation followed in frequency by the middle spindle (Fig. 2). Dilatation of the upper ureteral spindle was

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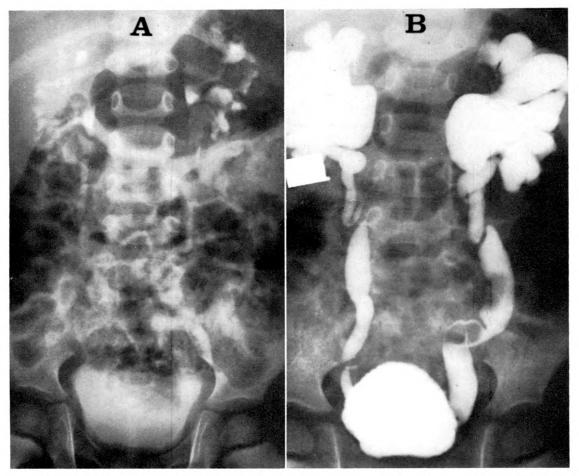


Fig. 1. Two and one-half year old male with one episode of urinary tract infection. (A) There is only mild dilatation of the collecting system in the intravenous pyelogram. (B) The refluxing cystogram reveals marked hydronephrosis and hydroureter. The ureters are dilated down to their entrance into the bladder. No obstruction was demonstrated by urethrography or cystoscopy. Reflux causes increased volume and decreased emptying rate of the ureter, thereby increasing and accentuating the ureteral dilatation.

almost always accompanied by dilatation of the middle spindle or of the entire ureter (Fig. 3).

Segmental and generalized dilatation of the ureter was associated with persistent filling (Fig. 4). The calyces and pelvis also showed persistent filling and, many times, dilatation, if the upper ureteral spindle showed ileus. The persistent filling was a manifestation of atonicity and ineffective peristalsis. The dilated, persistently filled segments of the ureter were completely without peristalsis for several minutes. The peristaltic activity which did appear periodically was ineffective in that it did not completely sweep the ureter clean and many times was reversed and returned the opaque fluid to a higher level.

Eighty patients who had intravenous pyelography for reasons other than infection were used as controls. Normally, the minor calyces receive opaque material from the papillary tubules in an almost continuous stream and remain filled to some extent throughout the period of maximum excretion. Periodically, they expel their contents into the major calyces which usually contract promptly and remain empty until receiving the next egress from the minor calyces. Lack of complete emptying

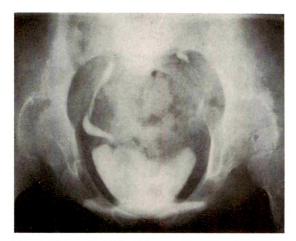


Fig. 2. Segmental dilatation and persistent filling of the lower third of the right ureter. This is caused by infectious atony. The opaque material remains in this segment for a long period of time. Fluoroscopic observation has revealed that it may finally empty into the bladder or reverse peristalsis may take the material into the upper ureter. There was no vesicoureteral reflux. The peculiar "double bladder" appearance is a normal variation caused by incomplete filling which allows the bladder vault to droop over the symphysis pubis.

of the major calyces, however, is not abnormal because in numerous patients they remain filled, apparently because the minor calyces empty so fast into them. This phenomenon is particularly prevalent during the maximum period of excretion. The major and minor calyces are sharp and distinct and show no dilatation even though they do remain persistently filled.

The normal renal pelvis acts as a reservoir for the major and minor calyces and may also remain filled during the peak excretion period. It expels a portion of its contents intermittently into the upper ureter. At times, it gets ahead of the flow from the calyces and may almost empty itself. There is no delayed emptying or over-filling of the normal pelvis.

The normal upper ureter receives the opaque material from the pelvis and quickly empties itself with good peristaltic action into the next lower segment. The peristaltic action is an orderly process in which the ureteral contents are rapidly

passed downward from one segment to another and into the bladder. This downward passage of the opaque material is sometimes so fast that it is difficult to follow by fluoroscopy. There is no segmental or generalized dilatation, atonicity, or persistent filling of the normal ureter.

Michie¹³ has stated that urinary infection damages the propulsive mechanism for urine flow, *i.e.*, the muscle in the infundibula, pelvis, ureter and bladder. Others^{3,6} have observed collecting system dilatation without obstruction but have concluded that it is due to reflux. In our group of 93 patients with nonobstructive dilatation,



Fig. 3. Segmental dilatation of the upper two spindles of the ureter bilaterally. This pattern is frequently seen with infectious ileus. There is invariably persistent filling, if not dilatation, of the calyces and pelvis when the upper spindle is dilated. Vesicoureteral reflux occurred on the right but not on the left.

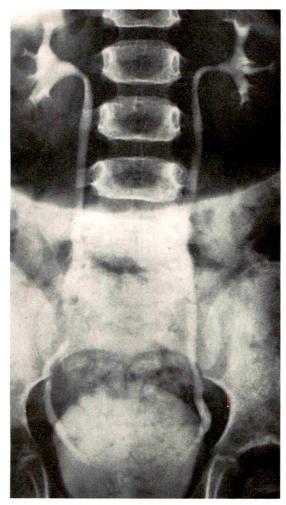


Fig. 4. Persistent filling and mild generalized dilatation of each ureter due to infectious ileus. There was no vesicoureteral reflux. The calyces and pelvis are not dilated but remained persistently filled. Decreased peristalsis due to ileus causes a reduction in the emptying rate of the ureter to account for the dilatation.

only 52 per cent exhibited vesicoureteral reflux by a method previously described. 16

The observation that infection causes dilatation has been experimentally shown by Jeffs and Allen.⁸ They established infection in 10 dogs without obstruction, and collecting system dilatation occurred in 7 but reflux in only 2. Nicolai¹⁴ provides further evidence of the dilating properties of infection by showing that much greater hydronephrosis occurs in an infected kidney

with a partially ligated ureter than in the noninfected one.

ELEVATED PRESSURE

The relationship of pressure to dilatation of the renal collecting system is difficult to assess. Pressure determinations were attempted as part of this study, using manometric and transducer recording devices. They were discontinued because observations based on these pressure studies revealed them to be extremely variable and unreliable, not only in the same patient during different examinations but also in the same patient during the same examination. Fluctuations of as much as 50 to 100 per cent were found in intravesical and intraureteral pressures at different periods of the same procedure. Even more striking fluctuations in the intravesical pressure were present in the bladder filled in a retrograde fashion by a catheter as compared to the one filled solely by ureteral emptying at the time of intravenous pyelography.

Many good studies of pressure and resistance within the ureter, bladder and urethra have been reported.^{2,3,11,12} These studies, likewise, reveal some variation of the pressure recordings, and clinical application of published data to nonobstructive dilatation of the renal collecting system is not possible.

The storage and passage of urine are highly individual and psychologic mechanisms. They vary in the same individual under different environmental, positional, and physiologic factors. Urodynamics are one thing when an individual is upright and alone and another when he is lying on a table with an audience.

Pressure within the renal conduits is also affected by peristalsis, volume, flow rate, voluntary and involuntary nervous reflex mechanisms, and psychologic states. These are factors which are impossible to control and raise the question as to whether pressure studies should be performed on the anesthetized or nonanesthetized patient. Some of the above mentioned factors would be controlled in the anesthetized patient

but the results, on the other hand, would be nonphysiologic and possibly lead to false conclusions. The results are equally nonphysiologic in the nonanesthetized, crying and struggling child in a strange and frightening environment.

Pressure is not the force which transports urine through the collecting system of the kidneys. A pressure of 80 mm. Hg would be required to drive the filtered fluid through the long and narrow convoluted tubules to the renal pelvis. Such pressures are not present. It is true that a Bowman's capsule pressure of approximately 30 to 40 mm. Hg exists as the filtration pressure. Resistance within the convoluted tubule reduces this pressure to between 1 and 5 mm. Hg, and the urine advances to the

calyces by capillary action created by tubular reabsorption.

Calyceal, pelvic and ureteral pressures of 0 to 5 mm. Hg have been reported by Kiil⁹ and Weinberg and Maletta.¹⁷ Peristalsis raises this temporarily to an average of 15 to 20 mm. Hg and is referred to by Melick *et al.*¹² as pumping pressure. Between peristaltic waves, the pressure returns to the lower normal level and no constant head of pressure is maintained.

While this experience with pressure measurements should make one cautious in forming physiologic and clinical conclusions, some useful information has been obtained in relation to nonobstructive hydronephrosis. For conciseness, the following observations are listed:

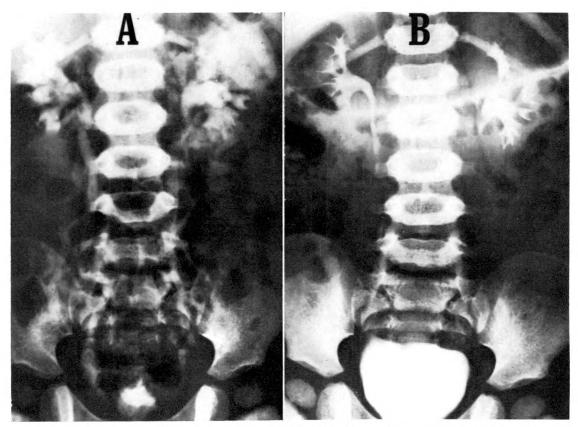


Fig. 5. Four year old male with pyelonephritis and cystitis. (A) Intravenous pyelogram showing generalized dilatation of the collecting system of each kidney due to ileus. There was no vesicoureteral reflux. Fluoroscopy showed poor peristalsis. The dilatation is caused by reflex ileus with the flow rate being raised above the emptying rate. (B) Intravenous pyelogram after 1 month of antibiotic therapy. The dilatation due to ileus has disappeared and normal peristalsis was observed at fluoroscopy.

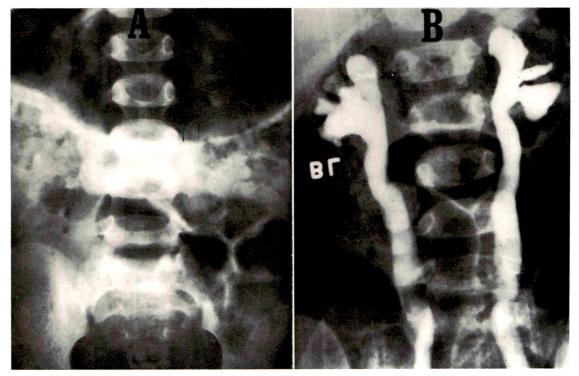


Fig. 6. Five year old female who had recurrent urinary tract infections over a period of 3 years. (A) The kidneys are poorly visualized but show only slight calyceal dilatation on the intravenous pyelogram. (B) Copious vesicoureteral reflux is demonstrated on the cystourethrogram and reveals the true extent of conduit dilatation. Reflux increases the volume and flow rate. The resulting functional obstruction causes dilatation of the expansible ureter.

- 1. Pressures in the nonobstructed, dilated ureter may be normal or high.
- 2. Pressures vary in the normal and dilated ureter as peristalsis passes through it, being higher ahead of the peristaltic wave. This is true whether the peristalsis is forward or reversed.
- 3. Ureteral pressures vary significantly from the bladder pressures, regardless of the presence or absence of vesicoureteral reflux.
- 4. Vesicoureteral reflux occurs at normal and elevated intravesical pressures.

Conclusions drawn from these observations must be preliminary and susceptible to change. They emphasize that factors other than obstruction are responsible for the pressure found in the nonobstructed hydronephrotic kidney and that the conduit dilatation in such kidneys may not be, or is only remotely, related to pressure.

FLOW AND EMPTYING RATES

The flow and emptying rates of a tube are closely related and practically the same if the flow rate is less than the emptying rate. The flow rate is largely determined by the volume of liquid regardless of its method of transportation. The emptying rate is controlled by the propulsive mechanism and the maximum lumen of the tube.

Fluid progresses uneventfully through a nonobstructed tube if its flow rate is less than the emptying rate. However, if the flow exceeds the emptying capacity, a functional obstruction is created because the tube cannot empty itself of all the fluid it receives. Dilatation occurs in such instances if the tube is expansible.

These principles may be illustrated by attaching a soft rubber tubing to a fluid filled syringe. The tubing maintains its integrity if the injection or flow rate is less

than the emptying rate. If, however, the injection rate exceeds the emptying rate, the walls of the tubing bulge even though no mechanical obstruction has been introduced. In other words, a dynamic obstruction has been produced.

This theory can also be applied to the ureter and helps explain nonobstructive dilatation of it. Infectious ileus of the ureter appreciably reduces its propulsive mechanism and emptying rate, and, when the latter is exceeded by the flow rate, ureteral dilatation results (Fig. 4; and 5, A and B).

Vesicoureteral reflux slows the emptying rate still further and also increases the flow rate by raising the volume of urine within the ureter. The adverse discrepancy between the flow and emptying rates and the resultant ureteral dilatation are, therefore, increased and accentuated (Fig. 1, A and B; and 6).

DISCUSSION

The observation that infection causes ileus indicates that there are new roent-genologic criteria for the diagnosis of pyelonephritis. Persistent filling with mild segmental and generalized dilatation of the ureter is the roentgenographic manifestation of ileus and atony. Garrett et al.8 observed segmental dilatation in some intravenous pyelograms of 30 patients who had nonobstructive vesicoureteral reflux. Gross and Sanderson4 earlier stated that dilatation of the lower third of the ureter in the intravenous pyelogram might be a clue that reflux would be found on cystography.

It is re-emphasized that mild segmental or generalized dilatation of the ureter is a sign of pyelonephritis. Reflux may or may not be present. It is readily admitted that reflux can be intermittent and not be demonstrated in a single cystogram. As mentioned earlier in this paper, reflux was found in only 52 per cent of the 93 patients with nonobstructive ureteral dilatation. Granted, reflux probably was not present in all of the other 48 per cent, but it may have been undetected in some of them.

Howerton and Lich⁷ firmly believe that infection is the cause of reflux. Schoenberg and associates¹⁵ have shown experimentally in dogs that infection alone can cause reflux. They crushed a 2 sq. cm. area of bladder muscle adjacent to an agar implant and the presence of cystitis was confirmed in all animals at autopsy. Nine of the 22 animals developed reflux secondary to the cystitis without detectable evidence of obstruction.

The observation that infection alone causes conduit dilatation supports the thesis that reflux is caused by infection since, in the past, obstruction and/or reflux have been predicated as being the cause of the dilatation. The invariably associated infection has been considered secondary, whereas there is good evidence that it should be considered primary. Obstruction and reflux can be secondary to infectious edema, spasm, ileus and fibrosis.

Ureteral compression has been recommended and used as a means of improving the quality of intravenous pyelograms. There is little doubt that enough compression can be obtained to cause some fullness of the renal collecting system which can simulate the mild changes of infectious ileus. The advisability of using ureteral compression is questioned and we have discontinued its use.

Nonobstructive, infectious dilatation disappears after the infection has been eradicated by antibiotic therapy unless irreversible changes have occurred as the result of reflux or inflammatory adhesions and stenosis (Fig. 5, A and B; and 7, A and B).

Persistent filling, fullness and mild dilatation of the collecting system are not necessarily specific for infectious ileus and atony. Similar changes have been noted with so-called compensatory hypertrophy of the kidney. The increased urine volume and flow in such a kidney have been observed to cause changes identical to those of ileus. Conditions causing increased urine volume and flow, such as diabetes insipidus and forced diuresis, seem capable of producing changes simulating infectious ileus. Hanley⁵ has reported dilatation of the

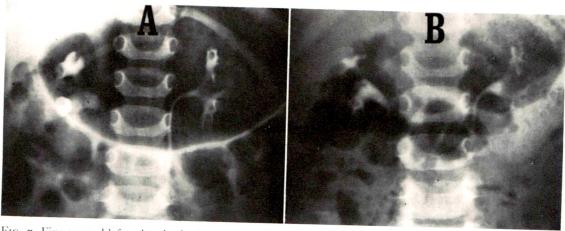


Fig. 7. Five year old female who had recurrent urinary tract infections on two occasions in a period of 6 months. There was no evidence of vesicoureteral reflux or organic obstruction on cystourethrography. (A) Intravenous pyelogram during the acute stage of the second infection. The calyces are full and blunted on the right. Ureteral ileus was demonstrated by fluoroscopy and on other films of the examination. (B) The calyceal dilatation has disappeared after 2 months of treatment with a sulfa drug.

box-shaped renal pelvis as the result of forcing fluids orally in patients.

SUMMARY

- 1. Nonobstructive hydronephrosis and hydroureter are caused by urinary tract infection.
- 2. The dilatation appears to be caused by reflux ileus and discrepancy between the flow and emptying rates of the renal conduits.
- 3. Clinical correlation of the pressures of the collecting conduits with the dilatation cannot be made.
- 4. Reflux increases and accentuates the dilatation.
- 5. Infectious, nonobstructive dilatation may disappear after antibiotic treatment.

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THE ASSOCIATION OF LUMBOSACRAL SPINE AND GENITOURINARY ANOMALIES WITH IMPERFORATE ANUS*

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PATIENTS with imperforate anus have a high percentage of associated lumbosacral spinal and genitourinary anomalies. 4,8,10,13,14,15,17,19,20 The latter are a major cause of morbidity and mortality, and frequently are not diagnosed until later in childhood when irreversible damage may have occurred to the kidneys.

Because of the close correlation noted between these serious urinary changes and the presence of spine abnormalities, it is important that neonatal abdominal roentgenograms taken for the diagnosis of "imperforate anus" be carefully examined for spine changes, and that, whether or not these be noted, a prompt urinary tract investigation (including intravenous pyelography and voiding cystourethrography) be carried out in the newborn period. 4,10, 13,17,19.20

The association of abnormalities in spinal differentiation, the coexistent errors in renal formation and bladder innervation, and the failure of normal formation of the rectum and anus all date to the crucial 5th to 7th week *in utero*. 1,5,8,13,14,15 At this time, not only is the cloaca dividing into the rectum and lower urinary tract but the kidney is forming in the presacral space from the metanephros. This "regional error in organization" impressed Duhamel⁴ in his studies of the association of imperforate anus to spine and genitourinary anomalies; he termed this association of defects the "syndrome of caudal regression." This grouping of anomalies, dated from the same period of development, is much more common than those of associated anomalies such as congenital heart disease, central nervous system malformations, etc.

SACRAL ANOMALIES

Varying degrees of sacral abnormalities are commonly present in patients with imperforate anus. 4,8,10,13,14,15,19,20 The range of deformity includes mild changes of sacral dysplasia (sacral stubbiness, sacral scoliosis) to varying degrees of actual segmental agenesis (Fig. 1, A and B). It is the presence rather than the severity of the sacral dysplasia that matches the urologic defects. Williams and Nixon¹⁹ have stressed the importance of sacral dysplasia in the diagnosis of neurogenic bladder with or without vesico-ureteral reflux; they commented on the high incidence of imperforate anus in this group of patients. Often the lateral study (Fig. 2, A and B) shows the abnormality to advantage. Actual total absence of the sacrum was not present in any of our patients.

The importance of the sacral defect is not in its need for spine support but in its coexistence with defective bladder innervation and poor development of the levator ani sling, including the central puborectalis and pubourethralis muscles so important for continence.2,13,15 The chance of an abnormal urinary tract is markedly raised in patients with imperforate anus who have sacral dysplasia. 4,10,15,19

Specifically excluded from this definition of sacral dysplasia is nonosseous fusion of the upper sacral segments, "spina bifida occulta." Since this is found in over 80 per

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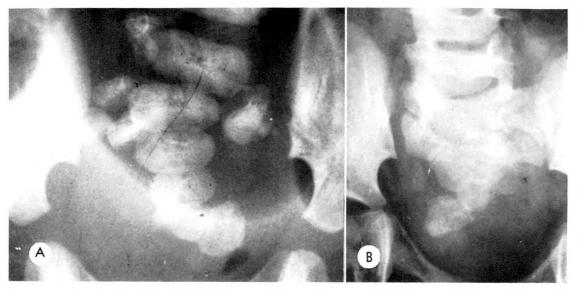


Fig. 1. (A and B) Sacral dysplasia. Though there are 5 sacral segments, they are malformed in shape and curvature.

cent of normal children, it is of no help and of no real meaning in patients with imperforate anus.¹⁹

LUMBAR ANOMALIES

Though much less stressed in discussions of spine defects in patients with imperforate anus, lumbar malformations are common.⁴ The more obvious defects, though not the most common, include gross

malsegmentation, hemivertebrae and even extra lumbar bodies (lumbar "epistasis").4

An unusual finding in a group of patients (all of whom proved to have the high type of imperforate anus as will be discussed below) was the narrowed lumbar "disk interspaces" at one to multiple levels. The interspaces were narrow anteriorly, creating a V-shaped interspace. "Disk space" actually is a partial term as it includes the

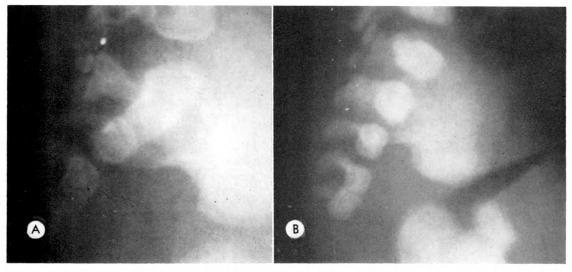


Fig. 2. (A and B) Sacral dysplasia. Lateral projection is often best for viewing the stubby inferior sacral segments as well as the abnormal curvature.



Fig. 3. Lumbar disk narrowing. The involved lumbar bodies point toward each other anteriorly, creating a narrowed V-shaped interspace.

nucleus pulposus and the growth cartilage capping the top and bottom of each vertebral body (Fig. 3). This finding was noted on the roentgenograms of a 9 year old girl, followed from infancy after an initial diagnosis of recto-vaginal fistula with imperforate anus and neurogenic bladder. The narrowed interspaces (Fig. 4) had been attributed variously to "infection" or "congenital" causes. When seen at 9 years of age, she had the typical tall waspwaisted block vertebrae; the sacrum was also abnormal.

Sequential changes of such disk space narrowing culminating in block vertebrae have now been seen in 8 patients. All these patients have had sacral dysplasia, usually of a mild type. All have had coexistent urologic defects, though no more severe than in those with sacral defects alone.

Six male infants have shown similar lumbar disk narrowing plus coronal cleft verte-

brae.^{3,12,16} These vertical lucent defects separated the vertebral body into a small posterior and large anterior segment; there was associated narrowing of the neurocentral synchondrosis (Fig. 5, A, B and C). The coronal clefts have disappeared in 3 to 6 months of follow-up though the disk space abnormality has persisted.

Coronal cleft vertebrae have been seen in normal patients without any anomalies; 3,12,16 however, in such cases the disk spaces are normal. Cohen, Currarino and Neuhauser3 noted that although the defects could be seen in otherwise normal patients, they were 3 times more common in association with congenital anomalies. The most common anomaly was imperforate anus. They made no specific comment on disk space narrowing, nor did they comment on the sex incidence. Coronal cleft vertebrae are 9 times more common in males,16 allowing a suggestion of prenatal sex determination on pelvimetry roentgenograms. All our patients with coronal cleft vertebrae and disk narrowing had the high type of imperforate anus and all were males.

Theories as to the cause of the clefts



Fig. 4. A 9 year old girl, who demonstrated the disk narrowing at birth, shows evolution of tall waspwaisted lumbar "block" vertebrae. An imperforate anus with recto-vaginal fistula had been repaired in infancy.

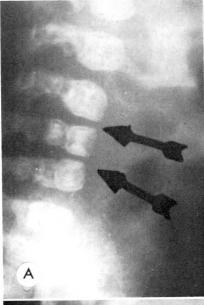
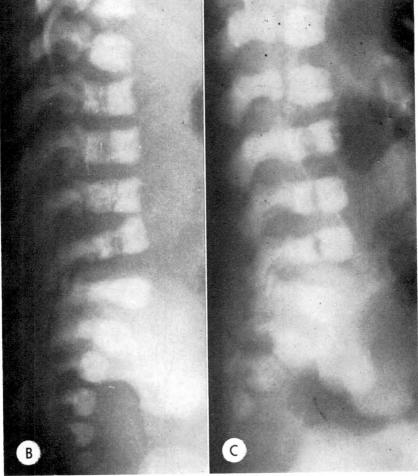


Fig. 5. (A, B and C) Coronal cleft vertebrae. All such patients were males with mild to severe coexistent disk space narrowing. The lucent coronal clefts disappeared in 3 to 6 months although the disk narrowing persisted.



have included persistent paired anterior and posterior ossification centers; this concept fails to explain the widened anteroposterior dimensions of the involved bodies. Cohen *et al.*³ found tissue in the clefts compatible with notochordal tissue. We believe the disk abnormality in these patients supports the notochordal remnant concept as a regional error in notochordal differentiation, as part of a larger regional error in caudal differentiation.

GENITOURINARY ABNORMALITIES

An increasing awareness of associated urologic abnormalities is apparent in contrasting recent reviews of imperforate anus^{4,5,8,10,11,13,14,15,17,20} with earlier important studies.⁷ This, in part, reflects improved urologic technique and earlier diagnostic studies. Most conveniently, the urologic findings are divided into structural and functional changes.

The functional changes constitute a major problem as they include vesicoureteral reflux and its sequelae of renal atrophy; this is often found at birth as the kidneys by then have been functioning for several months. The morbidity and mortality from unchecked renal damage exceed those of imperforate anus alone. 8,13,15,17,19 Most investigators of this type of renal abnormality 15,19 have implied a neurogenic deficit as the cause for the reflux and voiding difficulties.

The structural variations relate to renal formation (unilateral renal agenesis)4 (Fig. 6, A and B) and renal ascent (crossed fused and crossed solitary ectopia)9,18 (Fig. 7, A, B and C). They share in common some error in the normal formation of the kidney from the metanephros in the presacral space, its relation to the mesonephrically derived ureter and collecting system, a normal ascent from the pelvis with capture of the kidney by lumbar aortic branches and loss of the segmental vessels from the iliac arteries that are normally found at the fifth to seventh week in utero. If this regional error in organization is present, the kidney could

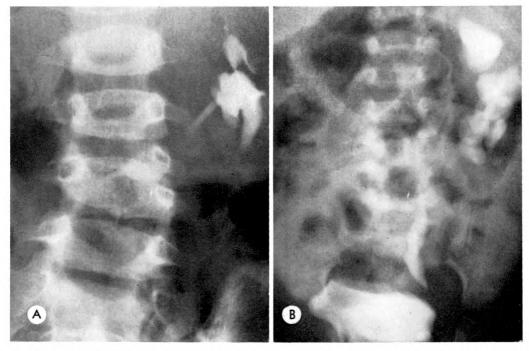


Fig. 6. (A) Unilateral renal agenesis. The solitary functioning kidney is malrotated but there is no vesico-ureteral reflux. (B) Unilateral renal agenesis. The solitary functioning kidney shows caliectasia and vesico-ureteral reflux is present.

either not form or form in an abnormal site with a persistent and thus anomalous blood supply. 9,18 Knowledge of such abnormal vessels and the accompanying problems of

renal and ureteral proximity to the site of planned surgery for imperforate anus are of obvious importance to the surgeon.

There is no reason why the functional de-

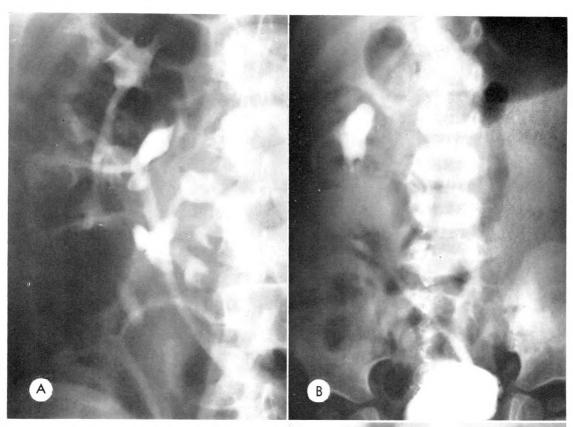


Fig. 7. (A) Crossed fused ectopia. This female patient had a recto-vaginal fistula with imperforate anus repaired in infancy. (B) Crossed solitary ectopia. This female patient had a recto-vaginal fistula with imperforate anus repaired in infancy. (C) Crossed solitary ectopia. Retrograde pyelogram through the single contralateral ureteral orifice found at cystoscopy of the same patient as in B.



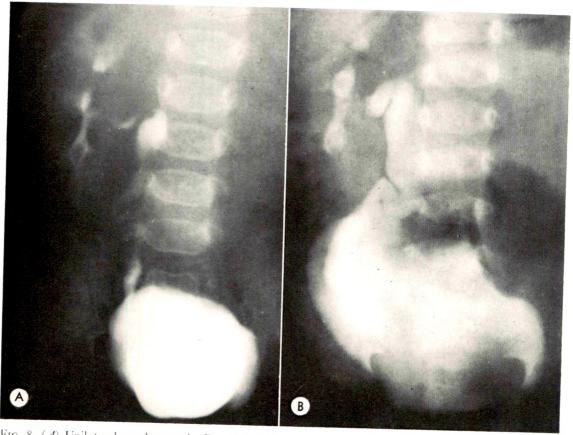


Fig. 8. (A) Unilateral renal agenesis. Remaining kidney shows good function without caliectasia on a 5 minute intravenous pyelogram. (B) One hour study as the baby was crying shows massive reflux to the sole kidney, confirmed later by a separate catheter voiding cystogram. Ileal conduit diversion was performed at 8 months of age.

fect of vesico-ureteral reflux cannot be superimposed on the structural anomaly of a single kidney, leading to the critical situation of a single refluxing kidney (Fig. 8, A and B). Thus, urinary tract evaluation in the newborn period is necessary before irreversible damage has occurred and certainly before major abdomino-perineal surgery is undertaken. Reflux may be identified by voiding cystourethrography which may be carried out by the intravenous route.

Where such diagnostic work-up has not been done, patients may present later in childhood or even adolescence with severe changes of hydronephrosis (Fig. 9A) or renal atrophy secondary to reflux (Fig. 9B). The latter patients all too often have been considered as having a "congenitally

hypoplastic kidney" when they actually are long-term cases of missed vesico-ureteral reflux with superimposed infection and atrophy. Careful dissection of the presacral autonomic plexuses by Stephens¹⁵ has been of limited success in actually identifying nerve anomalies of formation or course in these patients with presumed "neurogenic bladders." Unfortunately, the vesico-ureteral reflux has in many patients been of sufficient degree in the months prior to birth that there is nonfunction to severe damage of the kidney by the time the infant is born.

THE COMPLEX ANOMALY OF "IMPERFORATE ANUS"

When patients with imperforate anus are studied, it is clear that they represent a





Fig. 9. (A) Unsuspected massive hydronephrosis in a seemingly well 2½ year old boy whose imperforate anus was repaired in infancy without a urologic work-up. (B) Hypoplastic functioning kidney with subsequently documented vesico-ureteral reflux in a 12 year old girl whose imperforate anus had been repaired in infancy without a urologic work-up. The patient is normotensive.

group of malformations of differing severity, treatment and prognosis. The actual term "imperforate anus" is obsolete in the view of many pediatric surgeons, 4.5,8,13,15,19 suggesting as it does a mere membranous imperforation of the anorectum, one of the rarest of all anomalies (only I was found in 300 cases of "imperforate anus" at Babies Hospital).

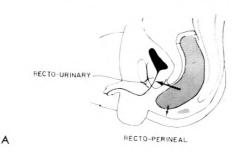
Recent major surgical reviews, with varying agreement, have placed the patients in 2 major groups, those with high and those with low lesions. 5,6,8,13,15,20 The high lesion cases are then classified by sex. Males with recto-urethral/recto-vesical fistulae are high; females with recto-vaginal fistulae are high. Patients without fistulae are high. All share in common a rectum terminating above the perineum, and usually above the levator ani sling. This failure of the rectum to penetrate the central part of the levator ani, the puborectalis sling, accounts for the significant incidence of incontinence in the best surgical hands until recent years.8,14,15 Most surgeons include low vaginal fistulae in the high lesion group for surgical rather than levator ani reasons of classification.

Both males and females in the *low* lesion group have fistulae to the perineum (ectopic perineal anus, anterior anus, covered anus, "recto-perineal fistulae") or rarely a membrane-covered anus. They share in common a visible though abnormal termination of the rectum. By contrast, the *high* lesions may manifest themselves by air or meconium leaking through the urethra or meconium coming from the female vagina. The *high* fistulae themselves are not on the perineum.

The importance of this distinction to the radiologist relates to the greatly different association of spinal and genitourinary abnormalities in the 2 groups (Fig. 10, A and B). Two-thirds of the males and females with high lesions have the spinal as well as the structural and functional urologic defects referred to previously. This complicates an already difficult surgical problem. The ratio is not 1:1, as some patients with

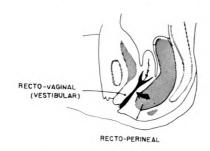
В

SITES OF "FISTULAE"



2/3 OF RECTO-URINARY HAD SPINAL AND GU. ANOMALIES
1/3 OF RECTO-PERINEAL HAD SPINAL AND GU ANOMALIES

Q SITES OF "FISTULAE"



2/3 RECTO-VAGINAL-(VESTIBULAR) HAD SPINE AND G.U. ANOMALIES NONE OF THE RECTO-PERINEAL HAD SPINE OR G.U. ANOMALIES

Fig. 10. (A) Relation of site of fistula to incidence of spine and urologic abnormalities in males. (B) Relation of site of fistula to incidence of spine and urologic abnormalities in females.

normal spines have urologic defects and vice versa, the spine, occasionally, may be abnormal, while the urinary tract appears normal. The males with low lesions have only one-half as many associated spinal and genitourinary abnormalities; this means a one-third over-all incidence. Unexpected in our patients was the failure to find any spinal or genitourinary defects in 75 females with low lesions. This seems to indicate a protective influence of the interposition of the Müllerian structures (uterus, upper vagina) between the urinary tract and rectum. No further explanation is currently known and we should still perform intravenous pyelography and voiding

cystography on females with *low* lesions (recto-perineal fistulae, etc.).

Duhamel⁴ formulated the theory of a "regional error in organization" in discussing imperforate anus. He described the "syndrome of caudal regression,"⁴ the most severe form of which is the siren mermaid monster, which lacks kidneys, has rectal atresia, spinal abnormalities and lacks a uterus and vagina. Our patients have exhibited milder but similar joined defects. It is tempting to speculate that the error occurs closer to 5 than 7 weeks of gestation, since the kidneys, the cloacal differentiation into the rectum and bladder, and the formation of the lumbar and sacral spine are simultaneously affected.

It is important to realize that rectourinary fistulae are not "urologic" anomalies. Instead, they are persistent communications in the male between the rectum and the bladder or urethra. Normally present at 5 weeks in utero, as the urorectal septum divides the cloaca, they represent a failure of the rectum to migrate inferiorly through the levator ani sling and posteriorly along the perineum to meet the developing anus. Cessation of this migration at any point constitutes one of the various types of "imperforate anus." Such fistulous communications with the posterior urethra above the external sphincter can be diagnosed by the presence of air in the male bladder on inverted neonatal roentgenograms (Fig. 11, A and B); the sacrum is usually dysplastic. The females with high lesions lack bladder air, as the termination of the rectum is at the cloacally derived lower vagina and not the bladder.

For the surgeon this classification is practically as well as theoretically important. *High* lesions require colostomy followed at a later date by abdominoperineal bringing of the rectum through the puborectalis part of the levator ani sling. §,13,15 The *low* lesions can be handled by a "cutback" from the fistula to the anus, the latter found by faradic stimulation. Cases with *low* lesions do well surgically in the restoration of continence;





Fig. 11. (A) Air in bladder of newborn male with recto-posterior urethral fistula. Note coronal cleft vertebrae and disk narrowing. (B) Air in bladder of newborn male with recto-posterior urethral fistula. Note deformed sacrum.

cases with *high* lesions until recently have shown a 75 per cent ratio of poor to total failure of bowel control.^{8,13,15} To this must be added the additional problems of damaged or destroyed kidneys, considerably more frequent in the *high* group.

For the radiologist, this classification is also important. Males with spine changes have twice as many high as low lesions; females with spine changes are in the high lesion group. The radiologist cannot possibly render a sensible interpretation of roentgenograms in patients with "imperforate anus" without knowing the sex.

Clues, such as bladder air in males, point to the specific diagnosis. The major role of the radiologist is to evaluate the coexistent anomalies in the spine and subsequently to document the urologic status. The level of the imperforate anus requires clinical assessment.

Thus, for practical as well as embryologic reasons, Duhamel⁴ was correct in considering these patients with "imperforate anus" as having a regional defect—a "syndrome of caudal regression." The radiologist's role is to co-ordinate these various anomalies, which all too often have been relegated to the urologist and the surgeon, frequently with one ignorant of the other's findings. 8,13,15,19,20

SUMMARY

"Imperforate anus" is a syndrome of anomalies of organization of the caudal end of the body, frequently involving the genitourinary tract and lumbosacral spine, as well as the normal formation of the rectum and anus.

In patients with imperforate anus, any type of sacral deformity or error in lumbar segmentation (with subsequent evolution of "block" vertebrae) should be reason for prompt urologic evaluation by intravenous pyelography and voiding cystourethrography in the newborn period. To fail to do so may lead to irreversible damage from reflux. The functional anomaly of reflux may be superimposed on structural malformations including unilateral renal agenesis,

DATA

Our indication for voiding cystourethrography is usually a recurrent urinary tract infection. A total of 68 voiding cystograms were obtained on 61 patients (Table 1). Seven of the studies were postoperative examinations. The patient was unable to void in 7 studies, an incidence of approximately 10 per cent. Most of these patients were subsequently cystoscoped and a cystogram was obtained under general anesthesia. We feel that the most important factor was too little or too much premedication in these 7 patients.

- 1. Twenty-five patients who fall into our normal group (Fig. 1) were examined; 7 of these had prior treatment by surgery or dilatation, but at the time of our study were considered normal. One false positive examination is included in this group. This was a patient who was thought to have a small posterior bar, but on cystoscopy this could not be confirmed. There were 2 patients in whom a false negative report was given; both had diffusely narrow urethras at cystoscopy but were called normal on the voiding cystogram.
- 2. Seventeen patients with an abnormal bladder outlet without vesicoureteral reflux (Fig. 2, A and B; and 3, A and B) were examined. Fifteen of these patients had bladder neck contracture, I had a median bar, and the last, the only one in this group



Fig. 1. Six second voiding cystogram of an 11 year old female patient who was considered to have a normal study. The bladder neck is normal and there is no evidence of vesicoureteral reflux.

that could not void, had a urethral valve at cystoscopy. One patient in this group, who was diagnosed as having both a bladder neck contracture and a stenosis of the distal urethra on the cystogram, at cystoscopy had only a bladder neck contracture. Three of these patients had had prior dila-

TABLE I

Group	No. of Patients	No. of Cysto- grams	Male	Female	Could Not Void	Per Cent of Total
. Normal	25	25	4	21	5	25/61 = 41%
. Bladder Outlet Abnormality without Reflux	17	20	3	14	I	17/61 = 28%
. Normal Bladder Outlet with Reflux	10	11		10	I	10/61=16%
. Bladder Outlet Abnormality with Reflux	9	I 2		9		9/61 = 15%
Total	61	68	7	54	7	

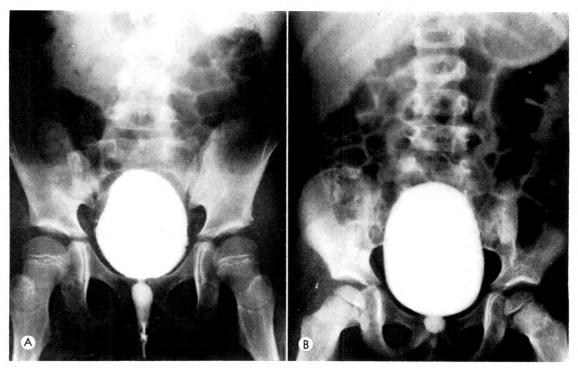


Fig. 2. Bladder outlet abnormality without vesicoureteral reflux. (A) Four second cystogram of a $6\frac{1}{2}$ year old female who had a bladder neck contracture with the typical deformity and poststenotic dilatation. Trabeculation of the bladder wall can also be seen. (B) 2.7 second cystogram of a 3 year old female with the same deformity. Roentgenographically it was thought that there was also a distal urethral stenosis, but this was not confirmed cystoscopically.

tations for their bladder neck abnormality. It is of interest in this group that 4 of the 17 patients had what we considered to be abnormal excretory urograms. Three of these showed slight ureteral dilatation and 1 showed a dilated calyx.

3. Ten patients, who had normal bladder outlet with vesicoureteral reflux (Fig. 4, A and B; and 5, A and B), were also examined. One patient in this group could not void but the cystogram with the bladder full showed bilateral reflux. Three of the 9 patients who voided had reflux only during voiding. One of these had reflux only on the last 2 films in the series and I only on the delayed film. In 4 of the remaining cases the reflux increased during voiding. Three of the 10 cases had abnormal excretory urograms consisting of intermittent ureteral dilatation. It is also of interest that 2 of these 10 cases had prior cystograms under general anesthesia which showed no reflux.

4. The last group consists of 9 cases with abnormal bladder outlet with vesicoureteral reflux (Fig. 6, A-C; 7, A and B; 8; and 9, A and B). Two false negative diagnoses about the bladder neck were made from the cystograms. One had edema of the bladder neck at cystoscopy but no fibrous or muscular contracture; I had a very mild bladder neck contracture, seen at surgery. This patient was not cystoscoped. Three of the 9 cases had reflux only on late voiding cystograms; in 2 of the remaining 6 the reflux increased during voiding. Two out of 9 cases had had prior cystograms under general anesthesia, showing no reflux. Six of the 9 had excretory urograms which we considered to be abnormal. Four of these, however, showed the changes of chronic pyelonephritis.

Other authors^{4,7,8,12} have demonstrated the signs on an excretory urogram which indicate the presence of reflux. In our se-

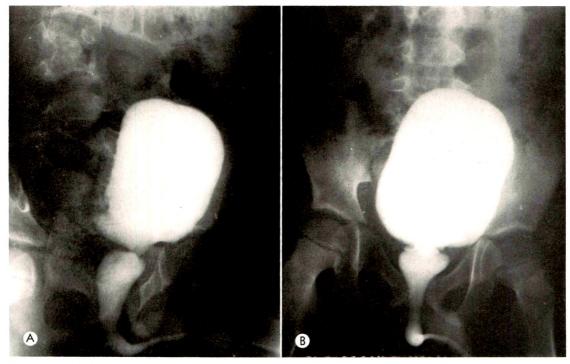


Fig. 3. Bladder outlet abnormality without vesicoureteral reflux. An 8 year old male with marked bladder neck contracture, mainly posterior. (A) 2.7 second preoperative cystogram. (B) 2.7 second cystogram after transurethral resection. The lumen through the area of contracture has been markedly increased.

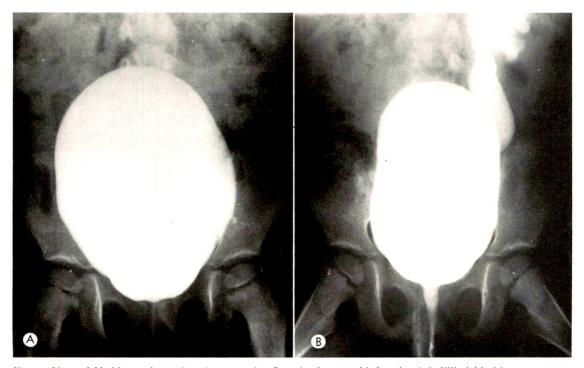


Fig. 4. Normal bladder outlet with vesicoureteral reflux. A $3\frac{1}{2}$ year old female. (A) Filled bladder cystogram shows no reflux. (B) 1.3 seconds after start of voiding. There is a massive left reflux present.

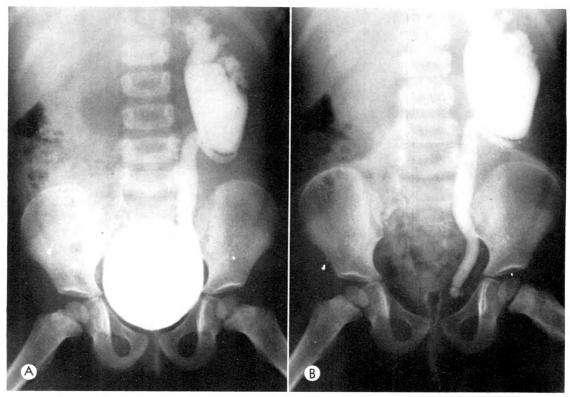


Fig. 5. Normal bladder outlet with vesicoureteral reflux. A $2\frac{1}{2}$ year old female. An excretory urogram on this patient I year prior had been called "very suspicious" of left ureteral reflux because the left ureter was slightly dilated and contained more contrast material on the postvoiding film. A cystogram under general anesthesia at that time showed no reflux. (A) Full bladder cystogram shows a massive left reflux with what we believe is secondary ureteropelvic type obstruction due to enlargement and rotation of the renal pelvis. The left collecting system and renal pelvis had been normal on the prior excretory urogram. (B) Ten second voiding cystogram at which time the bladder is empty. The left renal pelvis and ureter are larger and a diverticulum of the distal portion of the ureter can now be seen.

ries, undue distensibility of the distal onethird of the ureter and also signs of chronic pyelonephritis have been the most helpful in suggesting that reflux is present.

SUMMARY

Sixty-eight voiding cystograms were obtained on 61 patients with a rapid film changer. In 7 examinations, or approximately 10 per cent, the patients could not void.

Abnormalities were noted in 36 of the 61 cases, or 59 per cent. Bladder outlet abnormalities were demonstrated in 27 of the 61 cases, or 44 per cent, and vesicoureteral reflux in 19, or 31 per cent.

We feel that serial roentgenograms dur-

ing voiding are necessary because of our 19 reflux cases, 6 refluxed only during voiding and of the 6, 5 refluxed only at the end of the series or in a delayed study. It is also of interest to note that 4 of our 19 cases had prior cystograms under general anesthesia which showed "no reflux."

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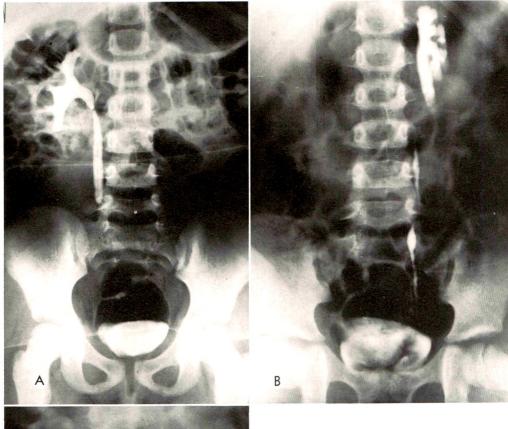




FIG. 6. Bladder outlet abnormality with vesicoureteral reflux. A 6 year old female. (A) Fifteen minute excretory urogram shows practically no function on the left side. A cystogram under general anesthesia on this patient showed no reflux. (B) Left retrograde pyelogram shows a small, atrophic kidney. A left nephrectomy was performed. The patient continued to have difficulty and 9 months later a voiding cystogram was made. (C) Filled bladder study shows reflux to the right kidney and also up the left ureteral stump. This patient had a mild bladder outlet contracture demonstrated on other films in the series.

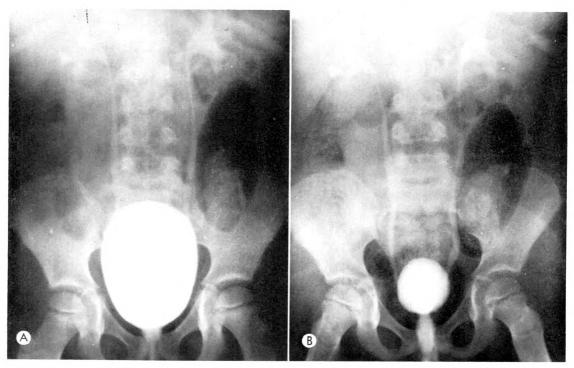


Fig. 7. Bladder outlet abnormality with vesicoureteral reflux. A 5 year old female. (A) Full bladder cystogram showing bilateral reflux. The bladder neck appears normal. (B) Ten second voiding cystogram. Mild to moderate bladder neck contracture can now be appreciated.



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FIG. 8. Bladder outlet abnormality with vesicoureteral reflux. A 2½ year old female. I.3 second study shows bladder neck contracture with massive right reflux. A late cystogram in the series also showed minimal left reflux.

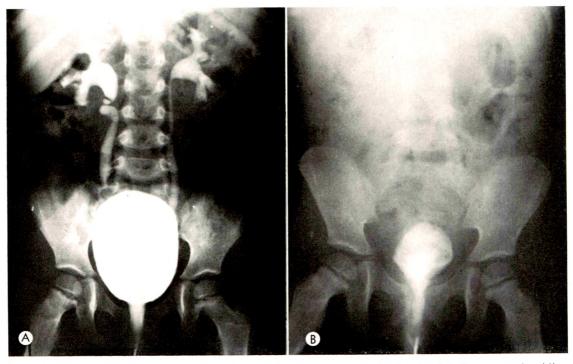


Fig. 9. Bladder outlet abnormality with vesicoureteral reflux. A 4 year old female. (A) Four second voiding cystogram shows bilateral reflux. The bladder neck was interpreted as normal but a mild contracture was found at surgery. (B) Four second voiding cystogram on the same patient following bladder neck revision and bilateral reimplantation of the ureters. There is a good outflow tract and no reflux. Postoperative excretory urogram was normal.

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URETHRAL DIVERTICULA IN WOMEN*

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URETHRAL diverticula in women can produce persistent and annoying symptoms and are often not discovered unless the lesions are specific considerations during diagnostic evaluation. Diagnosis of urethral diverticula in women has long been a difficult problem even though the urethra is the most accessible portion of the female genitourinary tract.^{3,4,7,8} Many clinicians feel that this is an example of a disease that is diagnosed in direct proportion to the intensity and perseverance of clinical and roentgenographic study.

The female urethra is a narrow membranous canal about 4 cm. long situated behind the symphysis pubis embedded in the anterior wall of the vaginal canal and directed obliquely downward and forward. It perforates the fascia of the urogenital diaphragm and ends about 2.5 cm. behind the glans clitoris. The lining membrane is thrown into longitudinal folds, one of which, lying along the floor of the canal, is termed the urethral crest. Many small urethral glands open into the urethra. The largest of these are the paraurethral glands of Skene, the ducts of which open just within the urethral orifice. Skene's glands in the female urethra are regarded as the homologues of the prostatic glands.

Opinion has varied as to whether urethral diverticula are congenital or acquired lesions. Support for the acquired nature of the majority of the diverticula is that the major symptomatic expression of the disease occurs in the 25 to 45 year old age group with rare cases diagnosed prior to the age of 20 years. Many investigators have postulated that infection and obstruction of the urethral glands result in formation of retention cysts which by suppuration or trauma, rupture into the urethral lumen giving rise to urethral diverticula. Most

clinicians today agree that these diverticula represent an acquired lesion of infectious etiology.

The common symptoms reported in the literature are: frequency, burning, dysuria, incontinence and dyspareunia.¹ Table 1 gives the distribution as encountered in our series. Dysuria and frequency were by far the most common symptoms.

Previous methods for female urethrography have relied upon simple injection of contrast material with a syringe inserted in the external meatus or single film documentation of the urethra during voiding after retrograde filling of the bladder. 5 A third method is to identify the orifice of the diverticulum at cystoscopy and inject contrast material directly into the orifice. A fourth method has been described as "positive pressure urethrography." A double balloon catheter occludes the urethra proximally and distally to the orifice of the diverticulum during injection of roentgenographic contrast material.2,6 In recent years, we have been impressed with cineroentgenographic documentation on 16 mm. film of retrograde filling of the urethra

TABLE I
SYMPTOMATOLOGY

Urethral Diverticula in Women Age Range 26–67 Years				
Total No. of Patients	27			
Dysuria	14			
Frequency	ΙI			
Burning	I			
Suprapubic pain	I			
Flank pain	I			
Dyspareunia	4			
Urgency	2			
Stress incontinence	8			
Urinary dribbling	4			
Asymptomatic	3			

^{*} From the Department of Radiology, St. Luke's Hospital, New York, New York.

and bladder followed by a voiding cinecystourethrography. During retrograde filling the diverticulum will often expand. The marked distensibility of the diverticulum is best appreciated with cineroentgenography which documents both the retrograde filling and the voiding phase of the examination. The degree of emptying and amount of retention of contrast material are documented and can be correlated with the clinical complaints.

The following cases illustrate the roentgenographic characteristics of this entity.

ILLUSTRATIVE CASES

Case I. This was the second hospital admission of a 43 year old woman who entered with the chief complaints of marked dysuria and stress incontinence. The patient had been well until 5 years prior to admission when she noted some abdominal discomfort with burning on voiding. In the last year the pains had become more persistent and burning on voiding with urgency had become more intense. Physical examination was unremarkable except for some vaginal discharge. The urethra was somewhat tender. No masses were felt.

In the hospital, cystoscopy and urethrography were performed. The urethrogram demonstrated a small diverticulum which appeared to originate in the mid-urethra (Fig. 1). With the bladder less filled, superior and inferior projec-



Fig. 1. Case 1. Urethrogram demonstrated a small diverticulum which appeared to originate in the mid-urethra.



Fig. 2. Case I. With the bladder less filled, superior and inferior projections from the diverticulum became more apparent.

tions from the diverticulum became more apparent (Fig. 2). Removal of the diverticulum is planned.

Case II. This 26 year old woman entered with the chief complaint of dysuria of 3 weeks' duration, accompanied by frequency, urgency and stress incontinence. Physical examination was essentially unremarkable except for some tenderness in the urethral area.

Cystoscopy revealed a tight meatal orifice. A urethrogram showed a pedicle with a wide lumen leading to the diverticulum (Fig. 3).

Case III. This 57 year old woman entered the hospital with the chief complaints of vaginal spotting for II months and a 20 pound weight

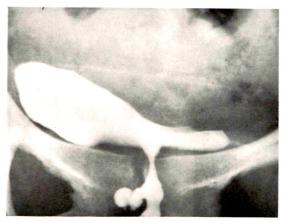


Fig. 3. Case II. Urethrogram showed a large diverticulum. Note the wide lumen of the pedicle leading to the diverticulum.

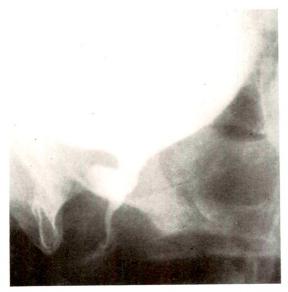


FIG. 4. Case III. Urethrogram revealed a small diverticulum of the urethra. This has remained asymptomatic.

loss. No urinary or rectal symptoms were present. Physical examination was unremarkable except that on pelvic examination there was a friable cervix with erosion and bleeding.

A cervix biopsy and dilatation and curettage were performed. The final diagnosis was squamous cell carcinoma of the cervix Stage II. The patient was treated with radium insertion and external irradiation and did well postopera-



Fig. 5. Case iv. Urethrogram demonstrated a diverticulum.

tively. A urethrogram revealed a small diverticulum of the urethra (Fig. 4). This has remained asymptomatic.

Case IV. This 38 year old woman entered the hospital with chief complaints of several months of frequency, dysuria, nocturia and dyspareunia. Past history was essentially negative. Physical examination was unremarkable. There were no signs of infection.

A urethrogram demonstrated a diverticulum (Fig. 5). The expansibility of the diverticulum was well shown on cine-examination (Fig. 14, A–D).

Case v. This 40 year old woman was seen in the clinic for intermittent vaginal bleeding. No urinary tract complaints were noted. A dilatation and curettage were performed for the patient's primary complaints.

Cystography and urethrography demonstrated an asymptomatic diverticulum (Fig. 6). The diverticulum remained well filled despite the empty urethra.

Case vi. This was the fourth hospital admission of a 45 year old woman who entered with the chief complaint of dysuria.

For the preceding 4 years, the patient had had varying degrees of dysuria with frequency



Fig. 6. Case v. Cystography and urethrography demonstrated an asymptomatic diverticulum. Note that the diverticulum remains well filled despite the empty urethra.



Fig. 7. Case vi. The patient was cystoscoped and minimal papillitis was demonstrated. A urethral diverticulum approximately 4 cm. from the urethral meatus to the right of the mid-line was noted. Late film after voiding phase showed retention of contrast material in the diverticulum.

and occasional hematuria. Three years before this admission, she had a transurethral repair of the bladder neck for papillitis, and at that time a urethral diverticulum was diagnosed. Since the symptoms had persisted, she was brought to the hospital at this time for removal of the urethral diverticulum.

The patient's physical examination was unremarkable except for pain associated with the left anterior vaginal wall.

The patient was cystoscoped and minimal papillitis was demonstrated. A urethral diverticulum approximately 4 cm. from the urethral meatus to the right of the mid-line was noted. A late film after the voiding phase showed retention of contrast material in the diverticulum (Fig. 7), which was lobular in shape. Under general anesthesia, the diverticulum was removed.

Case VII. This was the second hospital admission of a 41 year old Negro woman with the chief complaint of recurrent urethral diverticulum. One year prior to admission, the patient had a repair of a urethral diverticulum at another hospital. Since that time, she had had lower tract symptoms with pyuria and dysuria. She was seen in the clinic, at which time the urethral diverticulum was redemonstrated on

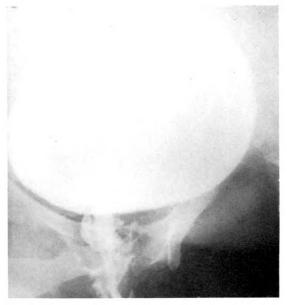


Fig. 8. Case vii. A urethral diverticulum was redemonstrated on cystoscopy and urethrography. The irregularity of the diverticulum suggests scarring from previous attempts at removal and/or inspissated material.

cystoscopy and urethrography (Fig. 8). The irregularity of the diverticulum suggested scarring from previous attempts at removal and/or inspissated material. Physical examination was unremarkable. No definite masses in the perior suburethral tissues were demonstrated.

The patient was taken to the operating room and the urethral diverticulum was removed. She has remained symptom free.

Case VIII. This 39 year old woman entered the hospital with the complaint of incontinence



Fig. 9. Case VIII. In the urethra, on the posterior wall, openings into the diverticulum were noted.



Fig. 10. Case 1x. Physical examination was unremarkable. Urethrogram showed 2 diverticula. Note the incomplete filling of the diverticula as compared to the well filled phase in Figure 11.

following a surgical procedure 10 years prior to admission. In the last year the patient had experienced frequency, urgency, hematuria, and pyuria.

Physical examination was unremarkable except that on pelvic examination there was tenderness in both lower quadrants of the abdomen.

A cystoscopy was performed and diffuse mild bladder inflammation was found. In the urethra, on the posterior wall, openings into the diverticulum were noted (Fig. 9). Expansion downward of the diverticulum in a course parallel to the urethra was seen. The diverticulum will be removed.



Fig. 11. Case IX. Well filled phase of diverticula.

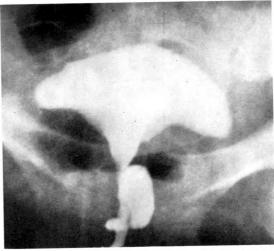


Fig. 12. Case x. A cystogram showed urethral diverticula. Multiple diverticula were not uncommon in our series.

Cine-documentation in this case is shown in Figure 15, A–D.

Case IX. This 43 year old woman entered the hospital with the chief complaints of frequency, dysuria, nocturia and microscopic hematuria of about I year's duration. Physical examination was unremarkable. A urethrogram showed two diverticula (Fig. 10 and 11). Figure 10 shows the incomplete filling of the diverticula as compared to the well filled phase in Figure II. Marked distensibility is often present. The patient was admitted and the urethral diverticula were removed.

Case x. This 49 year old woman entered the hospital for repair of a urethral diverticulum which was documented I year prior to admission. Approximately I year before, she had developed dysuria, frequency, nocturia, and burning on urination. A cystogram showed urethral diverticula (Fig. 12). Multiple diverticula were not uncommon in our series. The postoperative course was satisfactory.

Case XI. This 63 year old woman had experienced urinary incontinence and vaginitis. Cystoscopy and urethrography revealed urethral diverticula. Diverticula can involve the entire length of the urethra (Fig. 13).

Case XII. This 35 year old female entered the hospital with the chief complaint of mild incontinence, accompanied with frequency and pain-



Fig. 13. Case XI. Cystoscopy and urethrography revealed urethral diverticula. Diverticula can involve the entire length of the urethra.

ful urination. Cystoscopy and urethrography demonstrated a large multilobular diverticulum. The extensive involvement of this area was well demonstrated on cine-film (Fig. 16, A–D). Note the retained material in the diverticulum.

Case XIII. This 40 year old female entered the hospital with chief complaints of burning on urination, dysuria, frequency and nocturia. Urethrography and cystoscopy showed a diverticulum in the mid-urethral area. Cine-examination demonstrated satisfactorily the area involved (Fig. 17, \mathcal{A} , \mathcal{B} and \mathcal{C}).

SUMMARY

Diverticula of the urethra in women can be extremely variable in symptomatology, anatomy and disability to the patient. A diverticulum may be a completely incidental finding, or, at the other extreme, patients may suffer for several years with intermittent lower urinary tract infection with concomitant stress incontinence or urinary dribbling. The diverticula may be a few millimeters to several centimeters in

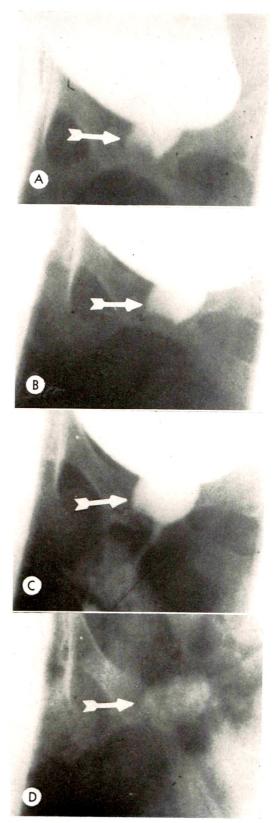


Fig. 14. Case iv. (A–D) The expansibility of the diverticulum was well shown in cine-examination. Good evaluation of the remaining urethra was possible. Retention of contrast material in the diverticulum was seen. (Note last frame of cinestudy.)

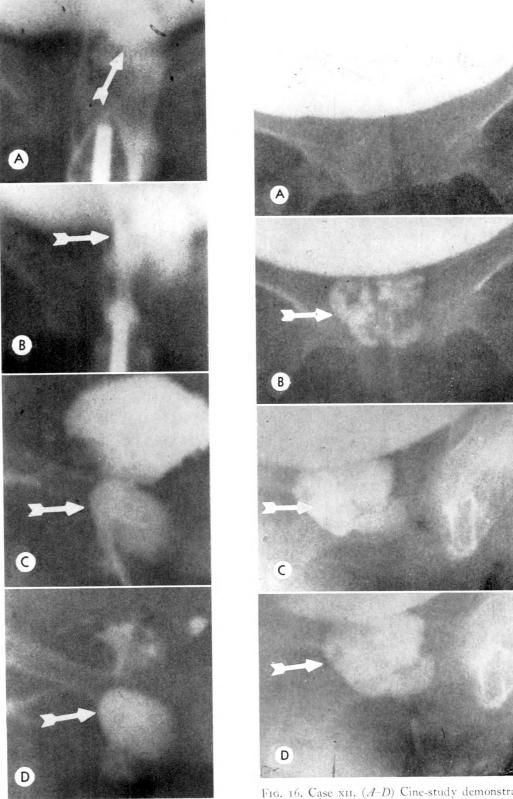
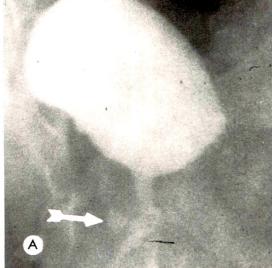
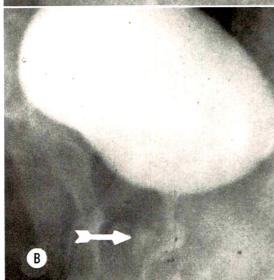
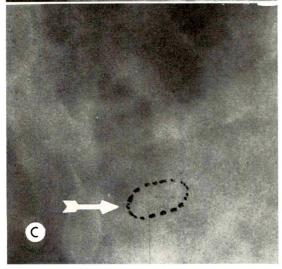


Fig. 15. Case VIII. (A–D) Cine-study of the urethra demonstrated the marked involvement of the periurethral soft tissue. The amount of potential pooling of urine was well shown. Frames A and B show retrograde filling of the diverticulum. Frames C and D are seen during the voiding phase.

FIG. 16. Case XII. (A-D) Cine-study demonstrated the large amounts of retained material in the diverticulum which became somewhat obscured when the diverticulum was well filled.







diameter. They may occur singly or several may involve the entire length of the urethra.

Many methods of filling the diverticulum with contrast material have been used. Documentation has varied from single roentgenograms to cineroentgenographic recording on 16 mm. film, the latter being the form we find extremely revealing.

Consistent diagnosis of this disease ultimately depends upon perseverance in clinical and roentgenographic study.

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We would like to thank Dr. Joseph Ward and Dr. John Draper for their help in the organization of the material and their clinical advice, and Mr. George Tanis and Mr. Thomas Wood for the printing of the selected cine-frames.

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Fig. 17. Case XIII. (A, B and C) Cine-study showed the diverticulum in the mid-urethra. (Note retention marked by arrow in C.

THE ROENTGENOGRAPHIC EXPLORATION OF TH PROSTATE AND THE URINARY BLADDER FLOOR VEINS*

PERIPROSTATIC PHLEBOGRAPHY: A NEW METHOD

By THEODOR LAUBENBERGER and HORST BERGHAUS HOMBURG (SAAR), GERMANY

PERIPROSTATIC phlebography enables the investigation of a region of the visceral veins of the pelvis in man. The periprostatic plexus and its collaterals in the urinary bladder floor can be visualized and information can be gained concerning the size and morphology of the prostate gland. Furthermore, the drainage of the venous blood from the prostatic gland and the urinary bladder floor can also be studied.

Various experiments have been carried out in an attempt to demonstrate roentgenographically the prostatic veins but were without success; aside from some of the bypassing veins, the periprostatic plexus was never filled.^{2,3,4}

TECHNIQUE

A cannula is inserted into the regic the perineum, as in a prostate gland p ture after local anesthesia. Then the t the cannula is manipulated to the d border of the prostate gland under directal control (Fig. 1a). After the puno of the periprostatic plexus, 40 per cent ble contrast medium* is injected a series of roentgenograms is made. The tient has no pain if local anesthesia is rectly given. Any perivascular deposi contrast material are quickly and pletely absorbed.

* "Urografin," Schering A. G

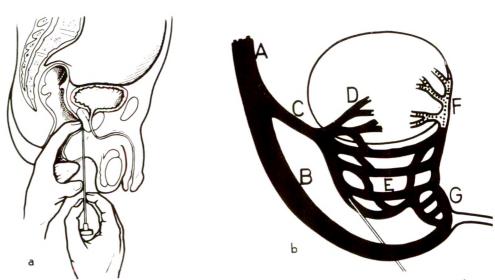


Fig. 1. (a) Puncture of the periprostatic veins. (b) Schematic drawing of the veins. A=vena hypog B=venae pudendae internae; C=venae vesicales inferiores; D=venae vesicales basales; E=perip plexus; F=vena vesicalis anterior; and G=vesico-pudendal plexus.

^{*} From the Department of Radiology, Director: Prof. Dr. F. Sommer, and the Department of Urology, Director: Prof. Alken, of the University of the Saarland.

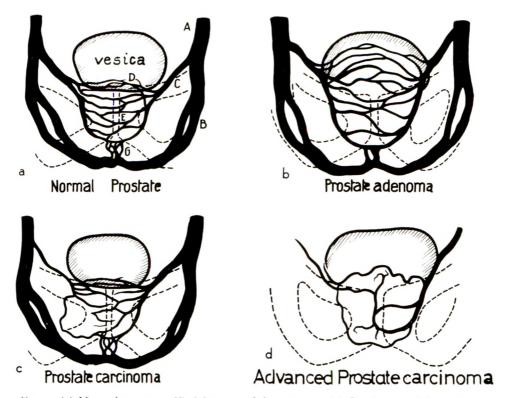


Fig. 2. (a) Normal prostate. (b) Adenoma of the prostate. (c) Carcinoma of the prostate. (d) Advanced carcinoma of the prostate.

ROENTGEN FINDINGS

The roentgenographic-anatomic relationship of the prostatic vein plexus, which has not previously been described, is shown diagrammatically in Figures 1b and 2a. The periprostatic plexus (E) surrounds the prostate gland. The main connections are the venae pudendae internae (B) and the venae vesicales inferiores (C). The injection of contrast medium results in a backflow into the dorsal urinary bladder base veins (D) and seldom into the vena vesicalis anterior (F).

Figure 2b, a sketch of a phlebogram in a case of adenoma of the prostate shows typical changes in the periprostatic plexus. The branches of the vena vesicalis inferior are cranially and laterally displaced. Vessel obstructions are not observed. At times, vessel rarefaction and stretching of the veins are demonstrated.

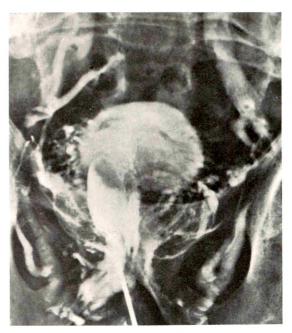


Fig. 3. Large adenoma of the prostate.

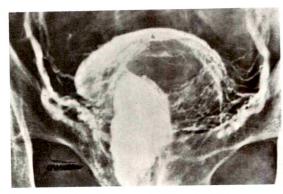


Fig. 4. Adenoma of the prostate.

Figure 3 is a phlebogram showing a large adenoma. The cranial and lateral displacement is significant. The extravascular contrast medium deposit was absorbed quickly.

A smaller adenoma of the prostate is demonstrated in Figure 4. The veins are stretched and their diameters are smaller than normal. The bladder lies caplike over the enlarged middle lobe of the prostate.

In carcinoma of the prostate phlebograms show vein occlusions, displacements and rarefactions (Fig. 2, c and d). The outflow of the contrast medium is delayed.

In Figure 5, vein obstructions of the periprostatic plexus, and of the beginning branches of the vena vesicalis inferior can be seen in a case of right-sided carcinoma of the prostate. In Figure 6, a large metastatic carcinoma of the prostate, the small periprostatic network appears as an irregular structure, with the veins differing in size.

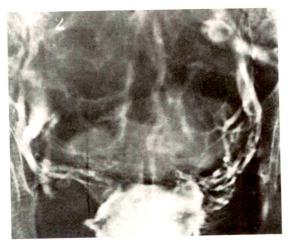


Fig. 5. Right-sided carcinoma of the prostate.

They are connected with the venae vesicales inferiores and with the thin vena pudenda interna sinistra. The floor of the contrast medium-filled bladder is irregularly contoured.

The periprostatic phlebography also permits an evaluation of the size and localization of tumors of the floor of the urinary bladder. In benign papillomas of the bladder pathologic vessel changes are usually absent. An example of a right-sided bladder papilloma can be seen in Figure 7, a and b. In contradistinction, carcinoma of the bladder always produces marked venous changes. Occlusions and rarefactions of veins can be noted on the bladder floor. In Figure 8, a and b, for example, most of the veins of the right dorsal border of the bladder are occluded due to carcinoma.

CONCLUSIONS

Periprostatic phlebography is a valuable roentgenologic technique in the evaluation of the prostatic gland and urinary bladder floor.

(1) By means of this procedure knowledge concerning the drainage of venous blood from the prostate gland and the urinary bladder floor can be obtained.

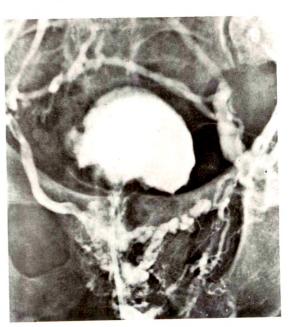


Fig. 6. Large carcinoma of the prostate.

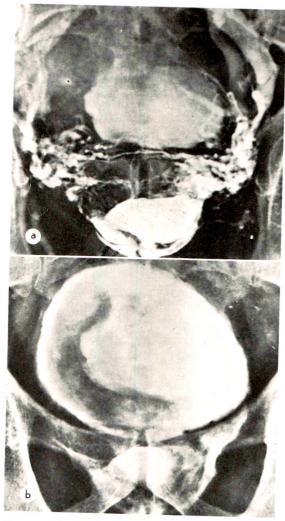


Fig. 7. (a) Phlebogram showing urinary bladder papilloma. (b) Filling of the urinary bladder.

- (2) Morphologic estimation of the prostatic gland is possible.
- (3) Typical changes in cases of prostatic adenoma, carcinoma or any other tumors of the bladder floor can be observed. This is of particular interest since this region has not been previously investigated by lymphographic methods.

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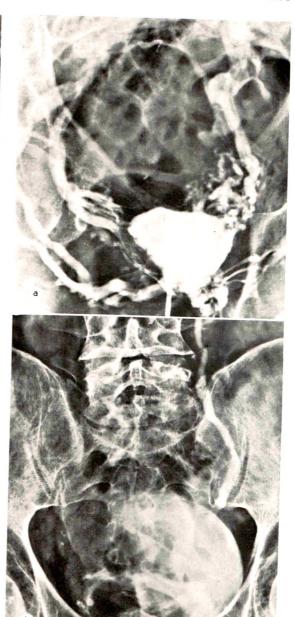


Fig. 8. (a) Phlebogram showing urinary bladder carcinoma. (b) Filling of the urinary bladder.

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TRANSLUMBAR RETROPERITONEAL CARBON DIOXIDE INSUFFLATION*

By E. EVERETT ANDERSON, M.D., and JAMES F. GLENN, M.D., F.A.C.S. DURHAM, NORTH CAROLINA

AHILL¹ in 1935 introduced unilateral retroperitoneal translumbar air insufflation for the delineation of adrenal tumors. but fear of renal injury, pneumothorax, and air embolism discouraged wide acceptance of this procedure. With the development of the presacral approach by Rivas in 1948, there was again a surge of enthusiasm for retroperitoneal air insufflation. During the interim this fervor has subsided because of technical difficulties, time required for the proper placement of presacral catheters, and the report by Ransom et al.3 of 58 deaths in 11,422 pneumographies following the use of air, helium, or oxygen. Despite their usefulness in the delineation of noninflammatory masses in the retroperitoneum, retroperitoneal contrast studies today are rarely used. It is the purpose of the authors to call attention to a rapid, simplified, and safe technique which has enabled them to obtain simultaneous bilateral translumbar retroperitoneal pneumograms in over 50 patients with a high degree of diagnostic accuracy and no morbidity.

METHODS

A laxative is given the evening prior to study. Fluids and food are restricted the following day and narcotics or barbiturates are administered for premedication. The patient is placed prone and semi-upright on a routine roentgenographic table (Fig. 1), and a preliminary plain roentgenogram of the abdomen is taken for renal position. The entire lumbar area is then prepared and draped as a sterile field, and local skin anesthesia is effected above the iliac crests and below the lower pole of each kidney. Twenty gauge lumbar puncture needles with stylets are introduced through the areas of anesthesia and directed slightly

cephalad toward the kidneys.5 Resistance is met at the transversalis fascia and when this is overcome, the retroperitoneal space has been entered. Stylets are then removed, and sterile Y-tubing of latex or plastic is attached to the needles and connected by a 3-way stopcock and rubber inhalation bag to a tank of 100 per cent carbon dioxide (Fig. 1). A 50 ml. Luer-Lok syringe is used to withdraw carbon dioxide from the tank for injection and a clamp is used to alternately occlude the arms of the Y-tubing. Injection of the gas is made into each retroperitoneal space until the patient experiences moderate discomfort. Such discomfort is felt in the average adult with approximately 300-500 ml. of gas in each retroperitoneal space. Injection of up to 1,500 ml. bilaterally has been accomplished

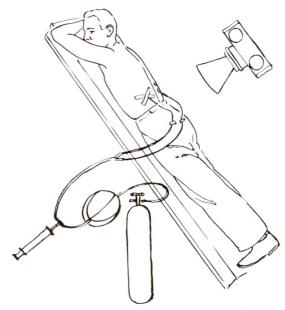


Fig. 1. Technique of simultaneous bilateral translumbar retroperitoneal carbon dioxide insufflation.

^{*} From the Division of Urology, Duke University Medical Center, Durham, North Carolina.

without complication. If the needles are inserted too superficially, subcutaneous emphysema with crepitus will be noted. Rapid roentgenographic exposures are made since carbon dioxide is rapidly diffused and absorbed. If the initial roentgenograms are unsatisfactory, further injections of carbon dioxide are done and further roentgenographic exposures are made.

DISCUSSION

For better delineation of retroperitoneal masses, pneumography is frequently combined with intravenous infusion urography. The procedure can also be combined with laminagraphy and arteriography. The use of any other gas other than 100 per cent carbon dioxide may be dangerous. The quality of contrast and the diffusibility of air, helium, oxygen, and carbon dioxide are essentially the same, but gases other than carbon dioxide are poorly absorbed and the possibility of gas embolism is omnipresent when they are used. Direct intravascular injection of carbon dioxide has long been employed in cardiac fluoroscopy without

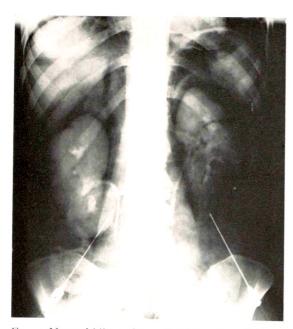


Fig. 2. Normal bilateral translumbar retroperitoneal carbon dioxide insufflation combined with drip infusion urography.

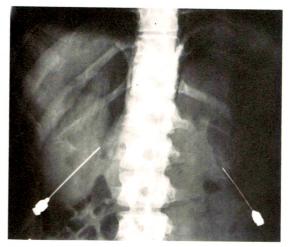


Fig. 3. Bilateral translumbar retroperitoneal carbon dioxide insufflation: aldosterone tumor of the right adrenal gland.

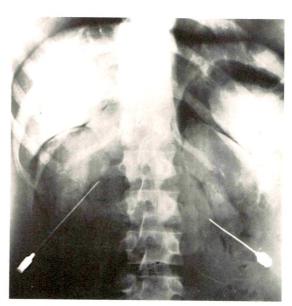


Fig. 4. Bilateral translumbar retroperitoneal carbon dioxide insufflation: right pheochromocytoma.

complications of gas embolism. In experimental animals, it is practically impossible to produce fatal gas embolism with 100 per cent carbon dioxide.² Although carbon dioxide is more rapidly absorbed by the retroperitoneal tissues, adequate studies may be obtained if film exposures are made immediately following insufflation. All of the insufflated carbon dioxide will be effec-

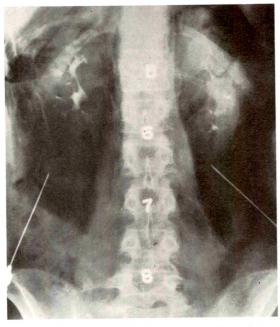


Fig. 5. Bilateral translumbar retroperitoneal carbon dioxide insufflation: bilateral adrenal hyperplasia.

tively resorbed within 30 minutes following injection.

Contraindications to retroperitoneal pneumography are previous retroperitoneal surgery, retroperitoneal inflammatory disease, and bleeding tendencies. The efficacy of this technique is illustrated in Figures 2 through 5. Figure 2 is a normal bilateral retroperitoneal pneumogram combined with a drip infusion urogram. Figure 3 shows an aldosterone tumor of the right

adrenal gland. Figure 4 demonstrate as right pheochromocytoma, and Figure 5 a bilateral adrenal hyperplasia.

CONCLUSION

A rapid, simplified, and safe technique for simultaneous bilateral retroperitoneal pneumography is described. This procedure has been performed in over 50 patients with a high degree of accuracy and no morbidity.

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THE DIAGNOSIS OF SUPRARENAL MASS LESIONS BY RETROPERITONEAL GAS STUDIES AND ARTERIOGRAPHY*

By ERICH K. LANG, M.D., MYRON NOURSE, M.D., JOHN MERTZ, M.D., DONALD McCALLUM, M.D., and WILLIAM NILES WISHARD, M.D. INDIANAPOLIS, INDIANA

RECOGNITION of the widespread and profound effects of the adrenal gland profound effects of the adrenal gland on all other organ systems has stimulated exhaustive studies of not only the function of the adrenal gland, but also primary disease entities and disturbances involving this organ. The clinician is challenged to diagnose abnormalities of the adrenal gland on the basis of biochemical findings, clinical manifestations, and in the recent past, classic roentgenologic presentation.

The authors attempt to prove the efficacy of special roentgenographic procedures in the diagnosis of suprarenal mass lesions. The appropriate use of roentgenographic studies, consisting of plain roentgenography of the abdomen, intravenous pyelography, upper gastrointestinal series, retroperitoneal gas insufflation, laminagraphy, arteriography, direct puncture of suspected cystic lesions with introduction of double contrast substances for further study of these lesions, scintiscanography of splenic tissue after sequestration of red blood cells tagged with chromium 51, and lymphangiography enables accurate and speedy diagnosis of such lesions.8,4,7,10,12,13, 14,15,17,19 A correct preoperative diagnosis was made in 57 of 66 patients examined with these modalities. In 7 more patients, the lesion was localized anatomically and its topographic relationship to the adjacent structures was recognized; however, its histologic nature was not correctly suggested.

DIFFERENTIAL DIAGNOSTIC CRITERIA

Masses in the suprarenal area include true lesions of the suprarenal gland, cysts

and tumors of the upper pole of the kidney, mass lesions associated with the spleen or accessory spleens, primary retroperitoneal tumors, hematomas, pedunculated cysts of the liver, tumors and cysts of the tail of the pancreas, aneurysms of branches of the celiac artery, tumors, and particularly, pedunculated tumors of the stomach, lymph node masses, and lastly, false shadows such as the fluid-filled gastric fundus simulating the presence of a mass. The true mass lesions of the adrenal gland can be of stromal, cortical, and medullary origin. The deliberate didactic step-by-step use of roentgenographic techniques should allow a precise differential diagnosis between these mass lesions.7

The presence of a mass is often suggested on a plain roentgenogram of the abdomen. Many lesions can be identified on the basis of typical calcifications, such as neuroblastomas, parasitic or hydatid cysts of the liver and retroperitoneal space, primary calcified tumors of the liver, and primary hydatid cysts of the kidneys. 12,15

Intravenous or retrograde pyelography, however, is, without doubt, the most important screening examination. The presence of a space-occupying lesion is suggested by a tilt of the axis of the kidney and depression or displacement of the kidney. The diagnosis of neuroblastomas or Wilms' tumors, suggested on the plain roentgenogram, is usually confirmed by the intravenous pyelogram. Cysts and primary tumors of the upper pole of the kidney are frequently correctly diagnosed on basis of characteristic splaying of the calyces and infundibula. Nephrotomography and renal

^{*} Presented at the Sixty-sixth Annual Meeting of the American Roentgen Ray Society, Washington, D. C., September 28-October 1, 1965.
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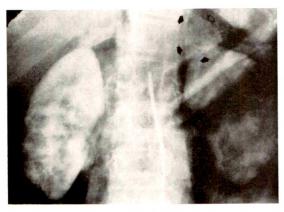


Fig. 1. A combined retroperitoneal gas study and arteriogram demonstrates a typical adenoma of the left adrenal gland. The adrenographic stain phase improves the clear delineation of the lesion. Note the bulge of the adenoma along the inferomedial border of the adrenal gland. The presence of the adenoma in this position was confirmed by surgical exploration.

arteriography may be opportunely employed to differentiate vascular and avascular lesions of the upper pole of the kidney.^{2,6,19}

Direct percutaneous needle puncture of cystic lesions of the upper pole of the kidney can be utilized to obtain fluid aspirate for biochemical and cytologic studies, and to introduce air and contrast material for further assessment of the wall of these cysts as well as exclusion of small tumors presenting within the cyst. Examination for presence of fat in the cyst fluid has been found a reliable criterion in the assessment of a cystic, necrotic, or shedding tumor.

The upper gastrointestinal series will unveil the most common fictitious lesion in the left upper abdominal quadrant—the fluid-filled fundus of the stomach. However, the properly performed upper gastrointestinal series will also be useful in the identification of primary tumors of the stomach, leiomyomas of the stomach, and particularly "iceberg tumors" of the stomach wall, presenting largely outside the stomach. Tumors and cysts of the tail of the pancreas are likewise suggested on the gastrointestinal series by their classic displacement of the stomach, and/or effect upon the "C" loop of the duodenum.

Scintiscanography of the spleen after intravenous infusion of red blood cells tagged with chromium 51, which will sequestrate in the splenic tissue, has proven particularly useful in identification of aberrant retroperitoneal splenic tissue, simulating an adrenal mass. However, the presence of such tissue is often suggested by the arteriograms.¹⁴

The retroperitoneal gas insufflation in association with laminagraphy remains the reliable standby diagnostic method for the radiologist. 5, 7, 8, 10, 11, 12, 13, 15, 16, 18 This technique allows topographic identification of the mass in relation to the surrounding structures; moreover, due to dissection it allows a true appreciation of the contour of the mass. The typical contour of certain adrenal masses permits a nearly histologic accurate identification of the lesion.8,11,12,13 For example, 8 patients with adenomas of the adrenal gland could be diagnosed on the retroperitoneal gas study (Fig. 1). The characteristic unilateral bulging of one of the walls of the adrenal is considered diagnostic of an adrenal adenoma. Adrenal hyperplasia is likewise a very characteristic lesion. Cushion-like bulging of all three walls of the adrenal suggests this diagnosis.8 This appearance is in a striking contrast to the concave borders of the normal adrenal gland: only the medial aspect of the normal adrenal gland may present with a convex border. Hemorrhagic (Fig. 2) and lymphangiomatous cysts of the adrenal gland may likewise exhibit a typical pattern. Most of them are quite large, round or oval shaped, and may show a nubbin-like projection of the displaced normal adrenal tissue along the medial and usually inferior border. Although calcifications presenting as spicule-like curvilinear shadows have been described, none has been seen in our series of 5 cysts.12 The hemorrhagic cysts usually appear as perfectly round and spherical masses; they are, in fact, pseudocysts secondary to infection, complicated by hemorrhage, which may result in rimlike calcifications. The lymphangiomatous cysts are felt to be caused by ectasia of the lymphatic vessels of the adrenal capsule and medulla, and contain a clear or straw colored fluid. Both hemorrhagic cysts showed the adrenal gland to be displaced to the inferomedial border, but clearly identifiable on the retroperitoneal gas study as a protuberance from the otherwise spherical mass.

Adrenal cortical carcinomas are more difficult to diagnose on the basis of their appearance on retroperitoneal gas studies. One of the patients examined in this series failed to show normal gas dissection in the retroperitoneal space (Table 1). This correlated well with an area of malignant infiltration of the surrounding tissues, demonstrated during surgical exploration. The other patient showed a polygonal mass with nodularity along the superior pole; moreover, the medial border of the mass could not be dissected off the inferior vena cava. Surgical exploration confirmed direct infiltration of the inferior vena cava by the tumor mass. Only I patient showed evi-

Fig. 2. The retroperitoneal gas study demonstrates a huge spherical mass above the right kidney, measuring more than 8 by 9.5 cm. in diameter. The right kidney is depressed; the axis of the kidney is tilted. The gas clearly outlines the circumference of this spherical mass and demonstrates separation from the upper pole of the kidney. Exploration confirmed the presence of a lymphangiomatous cyst of the right adrenal gland.

dence of faint calcification—a finding frequently emphasized in the literature^{7,11,12,15,17}

Metastatic lesions to the adrenal gland proved to show a characteristic pneumographic appearance in 7 of 14 patients. An eccentric, unbalanced, bulging lesion is felt to be typical of a metastatic implant of the adrenal gland. Lymphomas, bronchogenic carcinomas, and carcinoma of the breast appeared to show a predilection to present in this fashion. However, at least 2 patients with bronchogenic carcinoma of a total number of 6, showed a diffuse replacement of the entire adrenal gland.¹³

Arteriography may be opportunely employed to identify adrenal tissue by its characteristic adrenographic blush following the injection. 1,2,3,6,18 In combination with retroperitoneal gas studies and laminagraphy, it may be utilized to better identify and outline small adrenal adenomas or adrenal hyperplasia of Cushing's disease. The method, however, is most helpful and uniquely suited for identification of

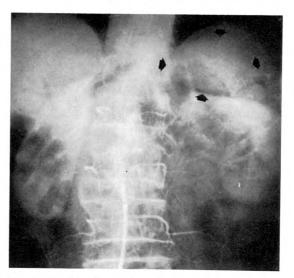


Fig. 3. The late phase of the aortogram demonstrates a 4 by 5 cm. large mass in the left suprarenal space, resulting in depression of the left kidney and tilt of the left kidney axis. During the injection, the patient sustained a severe hypertensive crisis, which was readily controlled by intra-arterial infusion of regitine. The presence of a chromaffin tumor of the left suprarenal gland was confirmed on exploration.

TABLE I SUPRARENAL MASS LESIONS ROENTGENOGRAPHIC EXAMINATION ASCERTAINING DIAGNOSIS

	No.	Plain Abdominal Roentgen- ography	Intravenous Pyelography	Gastro- intestinal Series	Air Study	Arteri- ography	Other
Primary Adrenal Lesions				4.00		· · · · · · · · · · · · · · · · · · ·	
Adrenal Adenoma	8				8		
Adrenal Hyperplasia	5				5		
Adrenal Cortical Carcinoma	2				2		
Pheochromocytoma	3					3	
Chromaffin Carcinoma	Ī					Ï	
Neuroblastoma	5	I	4				
Lymphangiomatous Cysts	2				2		2*
Hemorrhagic Cysts	3				3		3*
Metastatic Tumors to the Adrenal Gland							
Lymphoma	2				2		
Bronchogenic Carcinoma	6				4		
Carcinoma of the Breast	2				1		
Hypernephroma	3					3	
Carcinoma of the Colon	1						
Extra-Adrenal Masses Simulating							
Suprarenal Lesions							
Fluid in the Fundus of the Stomach	5			5			
Accessory Spleen	2					2	2†
Cysts of Upper Pole of Kidney	5					5	5 * ‡
Cysts in Tail of Pancreas	3			3	I	I	
Carcinoma of Tail of Pancreas	r					I	
Lymph Node Masses	4						18
Retroperitoneal Sarcoma	4	I					·

* Direct puncture of cyst with aspiration of fluid and double contrast study of the cyst.

† Scintiscanogram after intravenous injection of red blood cells tagged with chromium 51.

1 Nephrotomogram.

Lymphangiogram.

chromaffin tumors (Fig. 3).4,9,17 Pheochromocytomas show a very characteristic hypervascular pattern, with a dense sustained blush lasting for 3 to 4 seconds after injection of contrast material. Chromaffin carcinomas demonstrate a similar vascular blush. The examination is particularly valuable, since chromaffin tumors frequently involve extra-adrenal sites, including the intrarenal and subdiaphragmatic ganglia scattered from the renal hilus to the organ of Zuckerkandl. Only the arteriogram is capable of identifying chromaffin tissue preoperatively that might escape detection even during open surgical exploration. A hypertensive crisis may be provoked by the injection of contrast medium;

however, intravenous administration of regitine will readily check and control the blood pressure.9 Sustained hypotension following the examination may necessitate support with aramine.

Hypervascular metastatic lesions to the adrenal gland are likewise identifiable by arteriography. Hypernephroma metastases frequently favor adrenal implantation sites and may be readily identified by the corkscrew vessels disseminated throughout the adrenal gland, and the characteristic necrotic vascular pool formations (Table 1). Metastases of carcinoma of the thyroid also show a hypervascular pattern, but fail to exhibit the vascular lakes caused by necrosis in hypernephroma metastases.

Arteriography permits diagnosis of aneurysms mimicking a suprarenal mass lesion. In particular, aneurysms of the splenic artery and other celiac axis vessels may present in this fashion. Retroperitoneal angiomas show a fairly characteristic pattern on arteriographic examination.

Arteriography, in demonstrating the vascular supply, will further enable recognition of the topographic arterial relationship. For example, an accessory spleen defined on retroperitoneal gas studies can be identified as spleen because of its supply from the splenic artery.

Lymphangiography has been employed for demonstration of lymph node masses in the suprarenal areas. Unfortunately, adequate filling of these lymph nodes via injection of contrast material into the dorsal trunks of the forefeet is at best sporadic. Usually such masses cannot be opacified adequately, and only a characteristic lymphangiographic pattern of lymphoma, identified in lower para-aortic lymph nodes, will allow a conclusion by inference as to the etiology of the suspected suprarenal mass lesion.

DISCUSSION

The efficacy of roentgenographic diagnosis of suprarenal mass lesions was readily demonstrated in this series of 66 patients. By far, the most impressive diagnostic accuracy was obtained in primary lesions of the adrenal gland. The correct diagnosis of all cases of adrenal adenoma, adrenal hyperplasia, and adrenal cortical carcinoma was suggested on the basis of retroperitoneal gas study. The correct histologic diagnosis and location of all pheochromocytomas and chromaffin carcinomas was, likewise, suggested by the roentgenographic examination, and in particular by arteriography. Adrenal cysts, both of the hemorrhagic and lymphangiomatous type, were correctly diagnosed by means of aspiration and double contrast demonstration of the cyst. Five patients with neuroblastoma were diagnosed on the basis of calcifications seen on the plain roentgenogram of the abdomen and the characteristic appearance on the intravenous pyelogram.

The diagnosis of metastatic tumor implants of the adrenal gland was likewise readily made on the basis of special roent-genographic studies. Seven patients showed an eccentric bulging lesion involving either the upper or lower pole of the adrenal—a finding readily demonstrated by retroperitoneal gas studies. Two of these patients proved to have lymphoma (Fig. 4), 4 a



Fig. 4. The retroperitoneal gas study demonstrates marked depression and displacement of the right kidney. An oval shaped mass is occupying the midportion and lower pole of the right adrenal. A tail-like projection represents the upper pole of the adrenal gland. Histopathologic examination confirmed the roentgenographic impression of a metastatic lesion involving the lower pole of the adrenal and demonstrated classic lymphomatous infiltrates. (Reproduced with permission from the Journal of Urology, September, 1965.)

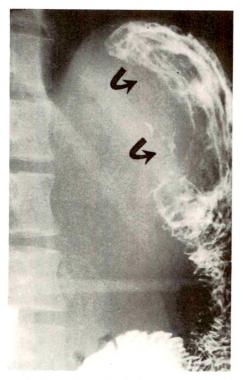


Fig. 5. A space-occupying lesion suspected on basis of marked depression of the left kidney on preceding intravenous pyelograms is diagnosed on this upper gastrointestinal study. Spicule-like calcifications and classic anterior and lateral displacement of the stomach stump suggest the diagnosis of a pancreatic cyst. Surgical re-exploration confirmed this impression.

bronchogenic carcinoma, and I a carcinoma of the breast. Seven patients showed irregular enlargement of the adrenal gland, with a nodular characteristic; 3 of these had a hypervascular pattern, with multiple corkscrew vessels, and areas of central necrosis on the arteriograms. A histologic diagnosis of metastatic hypernephroma could be suggested on the basis of this characteristic appearance. In 2 patients with metastases from a bronchogenic carcinoma, the diagnosis was suspected on the basis of the chest roentgenogram; however, the retroperitoneal gas study was not particularly helpful in assessing the histologic type of the adrenal lesion. A patient with carcinoma of the breast and I patient with carcinoma of the colon had each a large multilobular mass replacing the adrenal

gland, the appearance of which did not allow speculation as to the histologic type of the mass.

Extra-adrenal masses may frequently simulate true suprarenal lesions. The most common apparent mass in the left upper abdominal quadrant suggested on a supine plain roentgenogram of the abdomen is a collection of fluid in the fundus of the stomach. A gastrointestinal series will readily disclose the identity of such a fictitious mass, but laminagrams made in conjunction with retroperitoneal gas studies may be misleading. Accessory spleens often mimick the presence of a suprarenal mass. Demonstration of the blood supply originating from the splenic artery and, in particular, scintiscanograms identifying the presence of chromium 51 isotope deposited in the spleen after sequestration of red blood cells tagged with chromium 51, will help establish the diagnosis in such instances.

Cysts of the upper pole of the kidney were found in 5 patients of our series. In each case, the cyst was suspected on the basis of nephrotomography or renal arteriography, and a definitive diagnosis was made on the basis of double contrast studies, following direct puncture of the cyst and aspiration of fluid with replacement of this fluid by contrast material and air. Cysts of the tail of the pancreas are best diagnosed by upper gastrointestinal series (Fig. 5). The retroperitoneal gas insufflation and arteriography suggested the correct diagnosis in 1 of 3 patients. The fairly characteristic stretching of the splenic artery is felt to be diagnostic of the presence of a mass lesion in the pancreas. Carcinomas of the tail of the pancreas may be diagnosed on the basis of arteriography, showing a stretching of the splenic artery. Lymph node masses in the suprarenal area have presented the most difficult problem defying roentgenographic diagnosis. Only in I case of 4 could a definitive diagnosis be made on the basis of lymphangiography. Usually, lymphangiography will fail to visualize these high lymph node groups,

. 15:

particularly if performed in the standard fashion utilizing introduction of contrast material into the dorsal lymphatic vessels of the forefoot. A diagnosis can be made only by inference if other lymph nodes are found to be involved. Retroperitoneal sarcomas, in our series, also presented vexing problems in roentgenographic diagnosis. Only in I case was the correct diagnosis made on the basis of characteristic stippled calcifications in a huge mass. The relative avascularity, infiltrating nature, and homogeneous density of such sarcomas preclude a more accurate differential diagnosis by retroperitoneal gas studies or arteriography.

SUMMARY

The efficacy of special roentgenographic procedures in the diagnosis of suprarenal mass lesions is emphasized.

Topographically, the mass was correctly localized in 64 of 66 patients; in 57 patients a correct histologic diagnosis was suggested.

A systematic step-by-step application of the battery of special roentgenographic procedures is recommended for optimal diagnostic results.

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PHEOCHROMOCYTOMA CAUSING RENAL HYPERTENSION*

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DURING the past decade there has been an increasing awareness of the organic causes for arterial hypertension. Harrison et al.⁴ first described the association of pheochromocytoma and renal hypertension. Well known are the respective angiographic manifestations of pheochromocytoma^{1,3} and renal artery stenosis.^{5,6}

In the following case we have encountered both of these conditions at the same time in a hypertensive patient.

REPORT OF A CASE

This 36 year old white female was admitted to Emanuel Hospital with the chief complaints of hypertension and kidney disease. Hypertension had been diagnosed about ½ year previously as the cause of her headaches and visual disturbances. Her blood pressure reportedly remained labile under medical management, ranging from 140/90 to 190/130. Among a series of tests, excretory urography and a regitine test had been performed. All these tests had been allegedly normal with the exception of the finding of a mild obstruction at the left ureteropelvic junction.

The past history was of no relevance to this report with the possible exception of toxemia 6 years prior to this admission.

On this admission the patient's blood pressure varied between 190/100 and 260/150. The physical examination was essentially negative except for a bilateral bruit in the upper abdominal area. Laboratory data showed a normal hemogram; only a trace of albumin by urinalysis; 2–4 white blood cells and 4–6 red blood cells per high power field; creatinine 1 mg. per cent, and normal serum electrolytes, Urine culture failed to grow any pathogenic organisms. Catacholamines were 165 micrograms on a 12 hour specimen. A Stamey differential function test disclosed marked discrepancy in the volume of the urine excreted, with the left side

exceeding the right by 5 to 1. There was a concomitant significant disparity of para-amino-hippurate excretion, with greater concentration on the right. Retrograde pyelography revealed a smaller kidney on the right and definite narrowing of the left ureteropelvic junction without actual hydronephrosis (Fig. 1).

Aortography (Seldinger technique) utilizing a tip occluded catheter⁸ was performed for the purpose of anatomic mapping of the suspected renal artery stenosis. On the first series, the stenosis of the renal artery was well shown (Fig. 2); the lumen of the right renal artery was reduced about 3 mm. in diameter, approximately 35 mm. from the renal artery origin. Poststeno-



Fig. 1. Retrograde pyelogram. Stenosis at the left ureteropelvic junction without evidence of caliectasis. Some pyelectasis may be present. Extrinsic pressure upon the upper contour of the right kidney pelvis? Kidney displaced to the right?

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Fig. 2. Abdominal aortogram. First film of series. Right renal artery stenosis clearly outlined. Note: metal obturator within the catheter causing almost straight "face" of contrast agent in the abdominal aorta, thereby avoiding the filling of more proximally located branches.

tic dilatation was also noted. In the last roentgenogram of the same series (Fig. 3), a tumor stain indicated the presence of a tumor about 45 mm. in diameter. The tumor was nestled between the spine, the right kidney and the right renal artery below. In this series definite feeder vessels could not be shown to arise from the renal artery proper. A second injection through the catheter without the obturator proved that the major tumor arterial supply was derived from one large suprarenal artery (Fig. 4).

At surgery, the tumor was found lying in front of and medial to the upper pole of the right kidney with its greater surface under the inferior vena cava. The renal artery passed through the tumor. During the resection, the artery had to be sacrificed and was replaced by a 7 mm. dacron graft extending from the aorta to the distal renal arterial stump. Immediately following the removal of the tumor, the blood pressure fell to 90/40 mm. Hg, requiring the administration of vasopressors which restored the blood pressure to levels of 130/70 mm. Hg, at which it remained throughout sur-

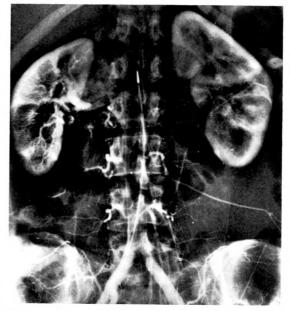


Fig. 3. Abdominal aortogram. Same series as Figure 2, 3½ seconds later. Tumor stain between right kidney and spine. Right kidney smaller than left by 16 mm.

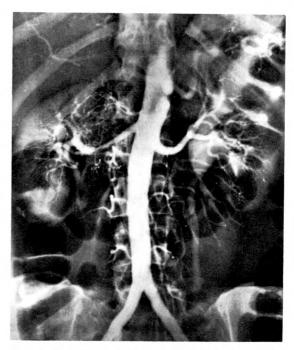


Fig. 4. Abdominal aortogram. Second series. Note: the obturator has been removed. There is now filling of the superior mesenteric artery and the celiac artery. The main arterial supply to the tumor is clearly demonstrated.

gery. The estimated amount of blood loss was in the order of 500 to 600 ml., replaced during the operation. At the conclusion of surgery, the blood pressure was stable.

On the third postoperative day, the patient had an attack of acute pulmonary edema secondary to left ventricular failure as a result of a blood transfusion and also toxic myocarditis. This was brought under control with tracheostomy, positive pressure breathing, diuretics, digitalis and phlebotomy. The patient recovered satisfactorily within a few days.

The pathologist reported pheochromocytoma.

DISCUSSION

Each of the conditions present in this patient by itself alone is capable of producing hypertension. Fate would have it that differential excretion test was positive while the regitine test had been negative. It is conceivable that the preoperative diagnosis of the tumor might not have been made had aortography not been performed. It must also be realized that the diagnosis could have been missed in spite of angiography (a) had a film series not been obtained or (b) if the tumor had been more proximally located, and the contrast agent delivered just at the level of the renal arteries as in translumbar aortography or tip occluded catheter. The answer in the latter case is obvious: A second injection should always be performed with the obturator withdrawn to fill the entire abdominal aorta with all its branches. Should then a mass or other lesion be demonstrated, necessitating more selective opacification, the obturator can be reinserted to guarantee a lateral escape of contrast agent and perfusion of the respective vessels with more concentrated medium.

Two cases similar to ours have been described. In Rosenheim and co-workers' case, renal artery stenosis was associated with a pheochromocytoma. At surgery it was found that the pheochromocytoma compressed the right renal artery. Yet, this patient differed from ours insofar as her renal ischemia had caused secondary hyperaldosteronism.

More recently, Garrett *et al.*² have reported a similar case in which, after removal of the pheochromocytoma, which impinged on the right renal artery, angioplasty was accomplished to revascularize the kidney.

SUMMARY

- 1. A case of pheochromocytoma causing renal arterial stenosis in a hypertensive patient has been described.
- 2. When using a tip occluded catheter, it is wise to do a second injection without the obturator (similar to selective renal arteriography) in order to opacify vessels originating proximal to the end opening of the catheter.

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ANGIOGRAPHY OF PHEOCHROMOCYTOMA*

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THE provisional diagnosis of a func-THE provisional diagnosis tioning pheochromocytoma is based on characteristic signs and symptoms and on the results of biochemical and pharmacologic tests. Because the tumor frequently cannot be palpated and because it may be multiple or extra-adrenal, the radiologist is called upon to localize it and to confirm its presence. In many cases, the classic signs and symptoms are not all present; the biochemical tests may be normal, and sometimes the diagnosis may not be suspected. Hypertension, for example, is a feature of pheochromocytoma but it may be sustained rather than paroxysmal. Because renal angiography has become a routine procedure in the evaluation of hypertension, a pheochromocytoma may occasionally be found unexpectedly. The radiologist, therefore, has to be familiar with the angiographic characteristics of pheochromocytoma and the hazards of the examination. Because of the tumor's rich blood supply, aortography is a diagnostic method by which pheochromocytoma can usually be diagnosed and localized.

Since 1962 a total of 5 cases of histologically proven benign pheochromocytoma has been studied by retrograde femoral aortography prior to operation. Serial films were exposed following injection of urografin.*

REPORT OF CASES

Case 1. A.O. (01 04 07), a 62 year old male, was admitted with a 35 year history of episodic attacks of nausea and vomiting and a 2 year history of hypertension (200/120). Palpation of the upper part of the abdomen provoked an immediate attack of nausea, vomiting and hy-

pertension. Urinary VMA (vanillylmandelic acid) was slightly elevated (10.5 mg./day).

At aortography (Fig. 1, A and B), a 12 cm. by 12 cm. richly vascularized tumor was found in the region of the right suprarenal gland, displacing the renal and adrenal arteries. No complications were encountered.

At operation, a 360 mg. pheochromocytoma was removed. The tumor was well encapsulated and histologically benign.

Postoperatively, the blood pressure (135/80) and VMA excretion (3.4 mg./day) were normal.

Case II. A.S. (13 10 29), a 51 year old man, had a 5 year history of intermittent tachycardia, a 3 year history of diabetes mellitus, occasional episodes of epigastric pain and a 1 year history of fluctuating systolic blood pressure (120–270). He was admitted because of paroxysmal attacks of hypertension (290/180) associated with severe headache, tachycardia and sweating alternating with episodes of shock.

A pheochromocytoma was suspected and an emergency retrograde femoral aortography was performed (Fig. 2, A and B). During the angiographic procedure, the patient had repeated attacks of hypertension alternating with periods of shock, only partly controlled by regitine† and hypertensin.‡ Aortography revealed a richly vascularized mass, 6 cm. by 6 cm., in the region of the right suprarenal gland. Shunting within the tumor was observed.

An emergency operation was performed. A 140 gm. benign pheochromocytoma was removed. After operation, the blood pressure returned to normal and the diabetes disappeared.

Case III. E.K. (09 04 20), a 53 year old female with an 8 year history of diabetes mellitus and hypertension (300/90), was referred for routine renal angiography.

Retrograde femoral aortography (Fig. 3, A

- † Trademark of Ciba for phentolamine hydrochlorine.
- ‡ Trademark of Ciba for angiotensin.

 $[\]sp{*}$ Trademark of Schering Corporation for diatrizoate methyl-glucamine.

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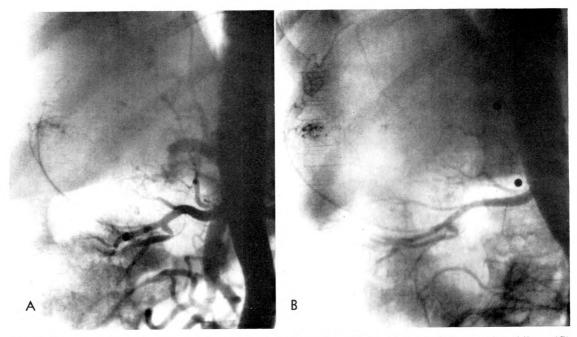


Fig. 1. Case 1. Abdominal aortograms, arterial phase, in anteroposterior (A) and left posterior oblique (B) projections demonstrate caudal displacement of the right kidney caused by a 12 by 12 cm. pheochromocytoma. The renal and suprarenal arteries are displaced. Adrenal arteries arising from the superior capsular artery, aorta and inferior phrenic artery supply the lesion. Tumor vessels are observed.

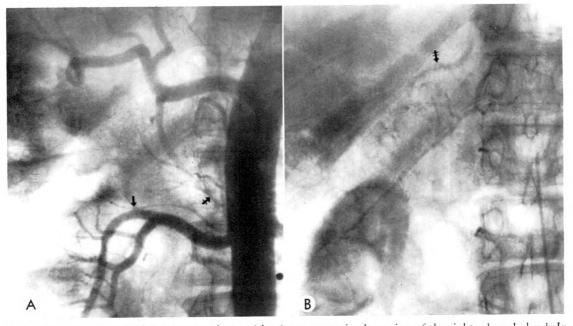


Fig. 2. Case II. Abdominal aortograms show a 6 by 6 cm. tumor in the region of the right adrenal gland. In the arterial phase (A) the superior capsular artery of the kidney (\rightarrow) is displaced downward as well as the kidney. Several middle suprarenal arteries (\rightarrow) are widened and displaced by the tumor. In late arterial phase (B) accumulation of contrast medium is observed within the tumor as well as abnormal vessels and early shunting of contrast medium to a wide vein (\rightarrow) .

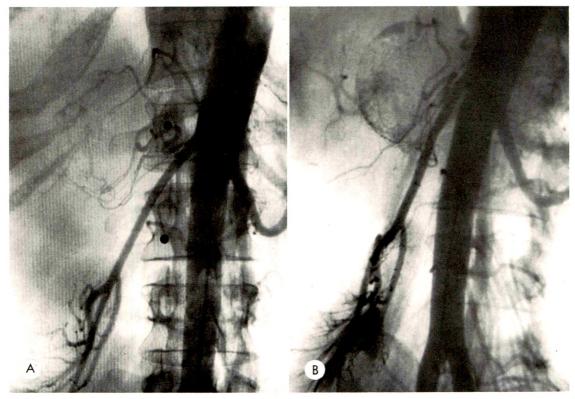


Fig. 3. Case III. Abdominal aortograms in anteroposterior (A) and right posterior oblique (B) projection show a 5 by 5 cm. tumor in the region of the right adrenal gland. The right kidney is ptotic but not displaced by the tumor. The arterial supply of the tumor originates exclusively from widened adrenal arteries arising from the right renal artery. The location of abnormal vessels and of the well circumscribed accumulation of contrast medium suggests an encapsulated pheochromocytoma.

and B) revealed normal renal arteries and a ptotic right kidney. In the right suprarenal region, a 5 cm. by 5 cm. richly vascularized, well encapsulated tumor was observed. The arteriographic procedure caused no complications.

Subsequently, a positive regitine test and a 24 hour output of 41 mg. of VMA were found, confirming the diagnosis of pheochromocytoma.

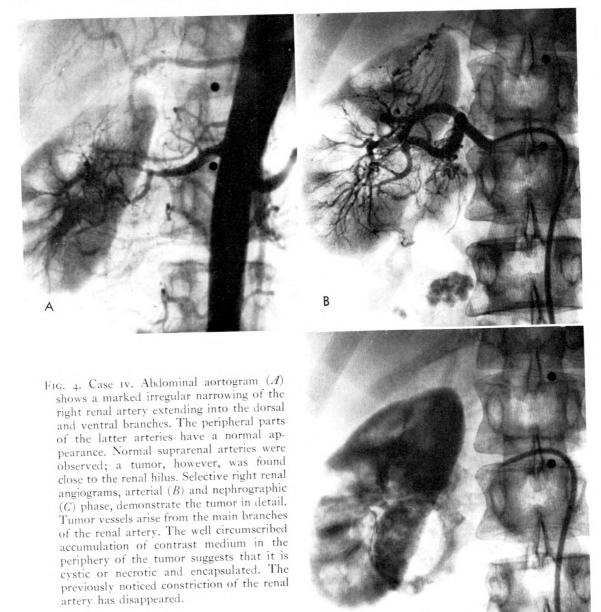
After removal of the benign pheochromocytoma, the blood pressure returned to normal (145/95).

Case IV. B.L. (170413), a 48 year old female with a 4 year history of hypertension, was found to have a loud bruit over the midabdomen and a 24 hour excretion of VMA of 7.5 mg. (normal).

A retrograde femoral aortogram (Fig. 4A) disclosed a marked irregular constriction of the distal part of the right renal artery and of the first parts of the dorsal and ventral branches.

The distal part of the branches had a normal appearance. Tumor vessels were observed medial to the renal hilus, while the suprarenal regions were of normal appearance bilaterally. In order to further evaluate the tumor, right selective renal angiography was performed (Fig. 4, B and C). The constricted appearance of the renal artery was no longer evident. The tumor was richly vascularized in the periphery while its center was avascular. The tumor, measuring 3.5 cm. by 4 cm. in size, was supplied by the right renal artery.

The tumor with the right kidney was removed. Histologically it was a benign pheochromocytoma with central necrosis. In the middle-sized renal artery branches, slight arteriosclerotic thickening was observed and in the larger branches small lipoid plaques within the intima and the media were noted. Slight pyelonephritic scarring was observed within the renal parenchyma. These pathologic changes were not marked enough to account



C

for the angiographic changes noted in the renal artery in the first examination. They could be the result of release of epinephrine from the tumor.¹

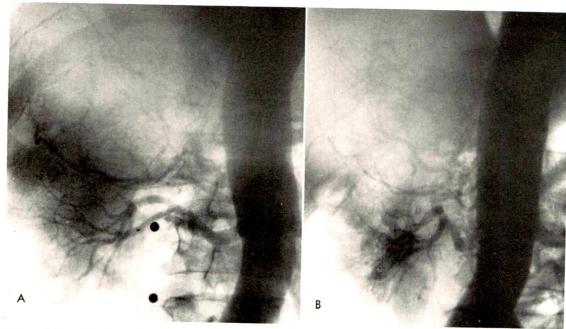
Postoperatively, the blood pressure returned to normal.

Case v. G.M. (010324), a 62 year old man with a 17 year history of hypertension and a 7 year history of mild diabetes mellitus, was admitted with an 18 month history of weakness,

excessive sweating, cardiac arrhythmias, increased appetite and a 12 kg. weight loss. The basal metabolic rate was elevated (+79 per cent) but thyroid function studies were normal. The blood pressure on admission was 230/135.

At aortography (Fig. 5, A and B) a large, richly vascularized mass was found in the region of the right suprarenal gland displacing the kidney caudally and laterally. No complications were encountered.

At operation, a 200 gm. tumor was removed



 F_{IG} . 5. Case v. Abdominal aortograms, left posterior oblique (A) and anterior posterior (B), demonstrate a vascular spheric mass in the region of the right suprarenal gland displacing the kidney laterally and caudally. The major arterial supply of the tumor is shown to originate from the aorta immediately above the origin of the renal artery.

and found to be benign. Postoperatively, the blood pressure returned to normal and VMA excretion was 4.3 mg./day.

FINDINGS

There were no serious complications following the arteriographic procedure, although one patient (Case II) had severe hypertensive crises before, during, and after the study. One of the patients (Case III) had an angiographic procedure because of hypertension. The diagnosis was first made by this study. The remaining patients were studied in order to preoperatively localize a clinically diagnosed pheochromocytoma.

The following angiographic findings were observed in our 5 cases, at least 3 of these 5 signs being noted in each case:

- 1. Abnormal vessels were observed in all cases within a mass located in the region of either of the adrenal glands (4 cases), or outside this area along the sympathetic chain (1 case).
- 2. When located within the region of the adrenal glands, the abnormal tumor vessels

originated from 1 or more of the 3 suprarenal arteries (4 cases).

- 3. Displacement of adjacent arteries or organs was observed in 4 cases.
- 4. A newly formed vascular bed was observed as an accumulation of contrast material within a well delineated tumor in 5 cases.
- 5. Premature filling of dilated veins draining the tumor was seen in 1 case.

DISCUSSION

Four roentgenographic techniques—plain film examination of the abdomen and chest, urography, nephrotomography, and inferior vena cavography—provide occasional indirect evidence helpful in the localization of a pheochromocytoma. For definitive study of a suspected case, however, it is now common to employ one of two techniques which yield direct evidence of a tumor—retroperitoneal pneumography or aortography. Retroperitoneal pneumography is accurate in the localization of suprarenal tumors in up to 80 per cent of cases (13 out of 16). Failure to localize

such tumors by pneumography is usually due to their extra-adrenal location or small size. In addition, clinically unimportant adrenal hyperplasia, periadrenal fat pad, anatomic variants, and postinflammatory changes may result in false positive pneumograms.

Because of the rich vascularity of most pheochromocytomas, aortography leads to a high percentage of accurate preoperative diagnosis and provides the surgeon with accurate information about blood supply. It is then possible for the surgeon to occlude the venous drainage of the tumor with minimal manipulation. Widespread utilization of the retrograde femoral approach for a variety of other purposes has led to a higher general level of technical competence and diagnostic skill in aortography than in retroperitoneal pneumography. At least 1 case has been reported in which the tumor, not detected by aortography, was subsequently demonstrated by pneumography.13 Symptomatic functioning tumors as small as 2 gm. have been described. We would not expect that a tumor of this size could be detected by angiography.10 This observation has led several authors to the conclusion that the procedures are complementary and to the recommendation by one author that the combined procedure is the method of choice.14 We believe that the added trauma of a routine combined procedure is not indicated.

The adrenal blood supply is extremely variable. It is composed of: (1) 4 to 30 superior adrenal vessels of small caliber from the inferior phrenic or its posterior division, (2) a middle adrenal vessel usually from the aorta but frequently aberrant or replaced by another artery, and (3) an inferior adrenal vessel usually of renal origin but in many instances of variable origin such as the aorta, superior polar, or capsular branch of the renal.24 This variability, together with the small size of all the arteries feeding the adrenal gland, accounts for the difficulty in detecting adrenal blood vessels when the gland is normal.14 The use of increased intrabronchial pressure to decrease the arterial flow

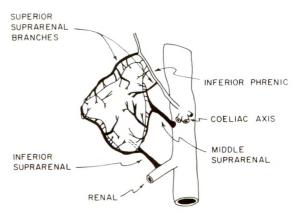


Fig. 6. Schematic arterial blood supply of the adrenal glands. (Modified from Merklin and Michels.²⁴)

can improve the demonstration of the suprarenal arteries.²² When the gland is enlarged by tumor, the demand for blood is supplied by an increase in size of one or more of the main arterial channels described above (Fig. 6).

It was possible to identify at least one of these channels in the 4 cases where the pheochromocytoma originated in the adrenal gland. Since some 10-23 per cent of pheochromocytomas originate in extraadrenal locations, 12 a careful study of the region of the sympathetic chain and the bladder should be made in cases in which no tumor is found in the adrenal area. A complete angiographic study would begin with injection into the upper lumbar aorta. If no tumor is discovered, the pelvic and thoracic aortas should be examined. Selective injection of contrast medium into the renal arteries often gives detailed information about the inferior suprarenal vessels.5 An aortogram is usually sufficient to make the diagnosis, but occasionally a selective renal arteriogram may be necessary to provide more detailed information (Case IV). The final diagnosis should always be based on clinical and angiographic findings since renal carcinomas may have the same rich vascular supply, abnormal vessels, and persistent accumulation of contrast material.

Three reports of fatal complications following translumbar aortography in patients

with pheochromocytomas 18,20,30 have probably retarded the use of aortography for the diagnosis of this type of tumor. Review of the literature since 19582,4,6-9,11-18,20-21,25-29,31 revealed 37 new cases of patients with proven pheochromocytomas subjected to translumbar or retrograde femoral aortography. Only 6 of these patients were reported to have had a hypertensive crisis during or following the procedure and there have been no reported deaths since 1958. The hypertensive crises reported were controlled by regitine or similar agents in the same manner as they are controlled during surgical removal. In the 3 fatal cases, the authors attributed the initiation of the terminal hemodynamic changes to the procedure and one of them concluded that its use in the presence of a functioning pheochromocytoma is probably contraindicated. 80 In all cases, there was a translumbar puncture of the aorta. It is possible that the blind technique of translumbar aortography could result in direct trauma to the tumor, a hazard not present when retrograde femoral catheterization is employed. Iodopyracet was used in all 3 cases. This agent is not now in general use because less toxic compounds have been developed. General anesthesia and multiple contrast injections were used in 2 cases. Since many mechanisms such as anesthesia, manipulation of the tumor, perirenal air insufflation or the slight trauma of a minor operative procedure may produce "adrenalin" shock in a patient with pheochromocytoma,3 it is clear that the general anesthesia employed in 2 cases cannot be excluded as a possible initiating cause of the hypertensive crisis.

Translumbar aortography should not be used for demonstration of lesions of the suprarenal gland. The retrograde femoral approach is less traumatic to the tumor and provides accurate control of the injection site, thus facilitating demonstration of extra-adrenal or multiple tumors. Retroperitoneal pneumography is as likely to provoke a hypertensive crisis in a labile patient as is retrograde femoral aortography. Because pneumography is less

likely to give a conclusive diagnosis than is arteriography, it should not routinely precede nor be combined with aortography. Rather, it should follow aortography when that procedure has failed to demonstrate a tumor. When performing either procedure, regitine should be available in the procedure room and the operator should be familiar with its use.

Hypertensive crises attributable solely to the retrograde femoral aortography did not occur in any of our cases. One patient (Case II) was admitted for emergency aortography because of a 48 hour history of repeated paroxysmal attacks of hypertension alternating with episodes of shock. These attacks continued to occur during the procedure, one following application of local anesthesia in the groin, one during puncture of the femoral artery and others throughout the procedure. The attacks also continued without interruption until surgery was performed in spite of partial control of the hypertension with regitine.

SUMMARY

- 1. The angiographic features of 5 cases of pheochromocytoma localized by retrograde femoral aortography are described.
- 2. Hypertensive crises attributable solely to the procedure were not encountered in these 5 cases.
- 3. To our knowledge, 42 cases (including the 5 in this paper) of pheochromocytoma have been studied by translumbar or retrograde femoral aortography since 1958 with 6 hypertensive crises and no fatalities.
- 4. Retrograde femoral aortography is relatively safe and is an effective method for the preoperative diagnosis and localization of pheochromocytoma.
- 5. Retroperitoneal pneumography should be reserved for the occasional suspected pheochromocytoma in which aortography does not demonstrate or adequately outline the tumor.

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LYMPHANGIOGRAM FOLLOWING HYSTEROSALPINGOGRAPHY*

By MARY STUART FISHER, M.D. PHILADELPHIA, PENNSYLVANIA

ALTHOUGH venous intravasation of contrast material during hysterosal-pingography is a well known and widely reported phenomenon, there has been little mention of uterolymphatic backflow in the radiologic literature. It is by no means rare, and, in several recent series published abroad, it has been described as being seen as frequently as venous spill.

The two conditions are difficult to distinguish when the small vessels of the wall of the uterus are filled, although the lymphatics are said to give a finer pattern, a blush of opacification. However, when the pelvic vessels are seen, it is easy to differentiate the two by the speed of flow, and opacification of lymph nodes on delayed roentgenograms definitely establishes the fact that lymphatic permeation has occurred.

Whereas venous filling is occasionally followed by respiratory symptoms and rarely by fatal pulmonary embolism, its lymphatic counterpart is apparently quite harmless.

Uterolymphatic intravasation was first described by Erbslöh³ in 1949. Drukman and Rozin² reported 62 cases in 1951, and Kika⁴ reported 52 cases in 1954. Like later workers, they found that the two phenomena often occurred together and were difficult at times to differentiate. Bourg,¹ in 1962, described 41 cases of lymphatic and 24 cases of venous intravasation and, in 1963, Mandruzzato et al.⁵ reported 46 cases of the two conditions.

Recent surgical trauma, improper technique with injury of the uterine mucosa, too much pressure applied in the presence of blocked tubes, and abnormal permeability of the uterine wall because of disease or an early phase of the menstrual cycle have

all been suggested as possible etiologies, and may be causative in producing venous filling. Bourg¹ implicated lipiodol, not having seen it after he changed to another contrast medium, but this has not been the universal experience. Many cases of both venous and lymphatic reflux have shown either hypoplastic, deformed, atrophic, or hyperplastic uteri—a wide spectrum. Most reported cases were in patients over the age of 30 years.

The lesion most consistently associated with lymphatic intravasation has been endometrial tuberculosis. This was true in 13 of Mandruzzato and co-workers' 46 cases, 32 of Kika's 52 cases and in a large proportion of those reported by Drukman and Rozin. The phenomenon was reproduced in several of Kika's cases when the study was repeated in different phases of the menstrual cycle.

Two cases are reported which were recently encountered at Philadelphia General Hospital.

REPORT OF CASES

Case 1. A 25 year old nulliparous Negro woman with complaints of menometrorrhagia, infertility, and abdominal pain had hysterosalpingography on the eighth day of her menstrual cycle. Ten cubic centimeters of ethiodol were injected. The uterus appeared normal, and the right tube filled with probable spill into the peritoneal cavity. In addition, there was early filling of a fine plexus in the uterine wall (Fig. 1), and the fluoroscopist terminated the injection when he realized that contrast material was flowing rapidly in extrauterine venous channels. Later roentgenograms demonstrated lymphatic channels on the left, with opacification of pelvic and abdominal lymph nodes at 24 hours (Fig. 2). The patient had no respiratory symptoms. Tissue from a dilatation and

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Fig. 1. Case 1. Ethiodol in veins, lymphatics, and uterine wall.

curettage performed the next day was reported as showing only proliferative endometrium.

Case II. A 26 year old Negro woman, with a



Fig. 2. Case i. Ethiodol free in pelvis, and in abdominal lymph nodes 24 hours later.

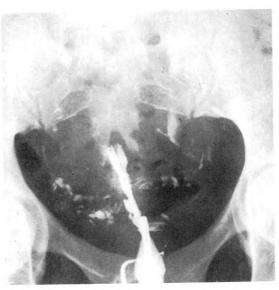


Fig. 3. Case II. Extrauterine ethiodol.

history of pelvic inflammatory disease 3 years previously, complained of menorrhagia and infertility. Hysterosalpingography done on the thirteenth day of the menstrual cycle required 6 cc. of ethiodol (Fig. 3). The contour of the bicornuate uterine cavity was somewhat irregular, and neither tube filled. A pattern of extravasation similar to that of the first case was seen, and delayed roentgenograms showed contrast material in the pelvic lymph nodes (Fig. 4). The patient experienced no ill effects. The



Fig. 4. Case II. Opacified pelvic lymph nodes on 24 hour roentgenogram.

following month, a tuboplasty was performed and a subserous fibroid was removed. The fimbriated ends were normal but the proximal tubes were adherent to the broad ligaments. No histologic or bacteriologic examination was performed.

SUMMARY

Two cases of uterolymphatic intravasation are reported.

Although no specific predisposing abnormalities were present in these instances, the majority of reported cases have been associated with endometrial tuberculosis.

It is suggested that this should be regarded less as a complication of hysterosal-pingography than as a sign suggesting a specific pathologic state.

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UTERINE LYMPHOGRAM FOLLOWING HYSTEROSALPINGOGRAPHY*

By FLORENCIO A. HIPONA, M.D.,† and THEODORE DITCHEK, M.D.‡

THE visualization of uterine lymphatics is an uncommon occurrence in hyster-osalpingography. 1-3,5-8,10,11 The purpose of the authors is to report a patient who had hysterosalpingography showing excellent opacification of the intrauterine lymphatic channels and corresponding extrauterine drainage. This provided an anatomic study of the lymphatic circulation of the uterus in vivo by roentgen examination.

REPORT OF A CASE

M. G. (47-49-69). This asymptomatic 26 year old Negro nullipara was admitted to the Yale-New Haven Hospital in 1965 to undergo hysterosalpingography as part of a sterility study. Her past history included a dilatation and curettage for dysfunctional bleeding in 1957, left oophorectomy and excision of a left ovarian fibroma via a posterior colpotomy in 1960, and an episode of acute pelvic inflammatory disease in 1962. Her menstrual cycle occurred every 21 days, lasting for 6–7 days. Physical and pelvic examinations were unremarkable.

Hysterosalpingography was performed under paracervical block, I week after her last menstrual period. The uterine cavity was normal. Both tubes were obstructed (Fig. 1A). During the injection of ethiodol, a mesh of lamellated small channels was seen in the uterus which represented intramural lymphatics (Fig. 1B). There was transient and minimal visualization of the left internal iliac vein. The injection was then stopped. Further roentgenograms demonstrated lymphatic vessels draining into the external iliac, hypogastric and presacral lymph nodes (Fig. 1C). The 24 hour roentgenogram revealed subsequent opacification of the common iliac and upper para-aortic lymph nodes (Fig. 1D).

The patient was asymptomatic during and after the procedure. Chest examination showed

no evidence of pulmonary embolism. Follow-up roentgen examination in 3 months revealed disappearance of the ethiodol from the lymph nodes.

DISCUSSION

According to basic anatomic studies,4,9 the uterus is endowed with a rich lymphatic network which has a lamellated appearance. The lymphatic retes of the endometrium, myometrium and perimetrium are closely interlaced with one another. The drainage of the cervix uteri is primarily by 3 major lymphatic pedicles, namely, the primary (cervical), the hypogastric, and the sacral, which terminate in the external iliac, hypogastric and sacral promontory lymph nodes, respectively. The lymphatic drainage of the corpus uteri is also by 3 major pedicles, vis., the principal (lumbar), the external iliac, and the anterior accessory (round ligament). These drain into the upper para-aortic, the external iliac and the inguinal lymph nodes, respectively.

In this case, the entire intrauterine and periuterine lymphatic plexus was well visualized. The major efferent pedicles drained into the external iliac, presacral and hypogastric groups of lymph nodes (Fig. 2 and 3). The intercommunicating lymphatic channels in the uterus facilitated cross drainage to other groups of lymph nodes ipsilaterally as well as contralaterally. On the 24 hour roentgenogram (Fig. 2) there was extensive fill of the upper para-aortic lymph nodes bilaterally at the level of the renal hili without significant opacification of the lower para-aortic lymph nodes. Thus, upper para-aortic lymph nodes are presumed to be filled directly from the prin-

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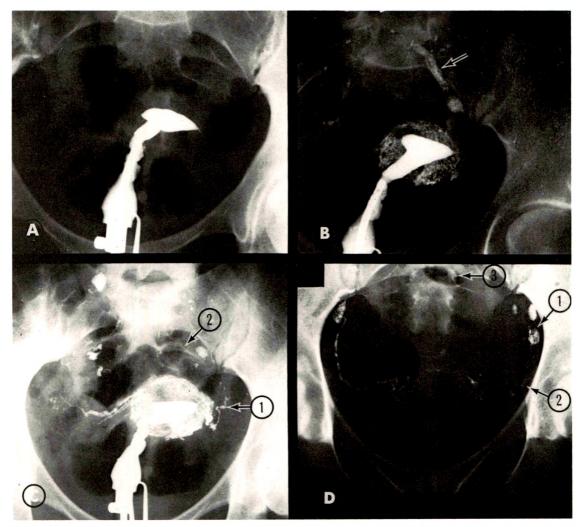


Fig. 1. Sequential studies from the hysterosalpingography with ethiodol. (A) The uterine cavity is normal. Only the proximal portion of the left tube is visualized. (B) The intrauterine lymphatics are seen in lamellar fashion with opacification of some efferent pedicles draining the uterus. There is minimal and transient opacification of the left internal iliac vein (arrow). (C) The major efferent lymphatic pedicles demonstrated are (1) external iliac and (2) sacral pedicles. (D) The 24 hour roentgenogram shows retention of contrast material in the (1) external iliac, (2) hypogastric and (3) promontory lymph nodes.

cipal (lumbar) pedicle of the corpus uteri bilaterally which normally drains into lymph nodes at that level.^{4,9}

In all but I case previously reported,⁶ the lymphatic opacification occurred with the use of oily contrast material in hysterosalpingography. Intrauterine pathologic states, such as tuberculosis, endometrial carcinoma and myomas, have been mentioned as predisposing factors for lymphatic visualization from the procedure.^{1,2,5,7,9} In

this case, as well as in others,^{3,10} the injection of oily radiopaque material (ethiodol) in the presence of bilateral tubal obstruction may have resulted in increased intrauterine pressure. This may be a factor in enhancing lymphatic intravasation.

The direct visualization of the lymphatics by modification of the standard hysterosalpingography may be a modality for investigation of the extent of uterine neoplasms.

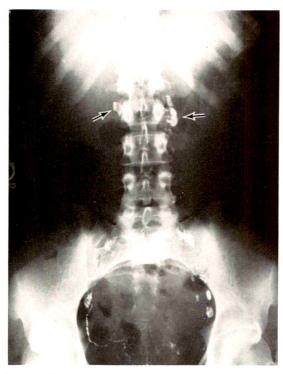


Fig. 2. The 24 hour roentgenogram of the abdomen demonstrates opacification of the upper paraaortic lymph nodes which are presumed to have filled from the principal (lumbar) pedicles of the corpus uteri.

SUMMARY

An *in vivo* roentgen study of the major lymphatic drainage of the uterus is presented. The factors involved in lymphatic intravasation are briefly reviewed.

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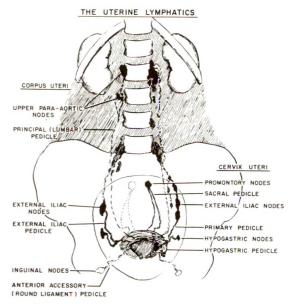


Fig. 3. Diagrammatic sketch of the uterine lymphatic circulation. The solid lymph nodes and pedicles represent the visualized primary drainage areas, the shaded lymph nodes are secondary drainage areas, and the open lymph nodes are nonopacified lymph nodes in our case.

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ROENTGENOLOGIC CHANGES IN UTERINE ISTHMUS INSUFFICIENCY*

By S. BRÜNNER and J. ULRICH COPENHAGEN, DENMARK

THE uterine isthmus is a complex sphincteric segment which connects the uterine cavity and the cervical canal. It is a narrow canal, about 10 mm. in length, ending proximally in the so-called anatomic os (orificium internum canalis isthmi) and distally in the so-called histologic os (orificium externum canalis isthmi) (Fig. 1). Microscopic examination of the mucosa at the external os shows that at this site the cervical epithelium has changed into one resembling the corpus mucosa, but thinner and containing far fewer glands, called the isthmic mucosa.

The views on isthmic function differ. Many authors assume that it has a sphincter action, both during the normal cyclic changes in the uterus and during pregnancy.¹

As early as 1948, Palmer and Lacomme⁶ felt that so-called isthmic incompetence was a common cause of miscarriage in midpregnancy or later. On the basis of this hypothesis, they performed some successful corrective operations on the uterine cervix. Later, Lash and Lash,³ Shirodkar⁷, and McDonald⁵ also treated this condition surgically.

The diagnosis of isthmic incompetence is made on the basis of: (1) A history of one or more miscarriages in mid-pregnancy or later. Characteristically such a miscarriage is preceded by sudden rupture of the membranes, little bleeding, and practically no pain. (2) Inspection and possibly palpation of the cervix in mid- or late pregnancy shows it to be effaced, and, at times, the intact membranes have prolapsed. (3) In nonpregnant women suspected of having isthmic incompetence, the free passage of Hegar dilators might lead to an impression, but not an exact diagnosis.

Bergmann and Svennerud, in 1957, made the diagnosis by inserting a Foley catheter. After the balloon had been expanded with 1 ml. of water, spring traction was applied. In this manner an impression was obtained of the power required to pull the catheter out of the cervix.

ROENTGENOGRAPHIC METHODS

Various roentgenographic methods have been used to visualize the isthmus. Among these have been conventional hysterosal-pingography¹ and the so-called isthmography employed by Youssef,⁸ who used a special rubber-lined blunt obturator (hysterosalpingography with an obturator provided with a vacuum disk has, in principle, the same possibilities of visualizing the isthmus).

In 1960 Hervet, Trocellier and Chicha, in Paris, described hysterography performed with the aid of a balloon. They introduced a balloon catheter and under manometric control expanded the balloon with contrast medium. As the balloon filled, the uterine cavity as well as the cervical canal became visualized. These authors concluded that the method was well-suited for determining the tonus in the cervical canal.

PRESENT METHOD

Since 1961, Mann and his associates⁴ have used a balloon catheter which was particularly well suited for demonstrating the isthmus. We have employed this balloon catheter in the examination of some habitual aborters. It consists of an unyielding, long rubber tube, ending in a yielding latex balloon. This balloon is made of two parts, a head of thin latex and a neck of somewhat thicker latex (Fig. 2). By means of a mandrin, the catheter is introduced

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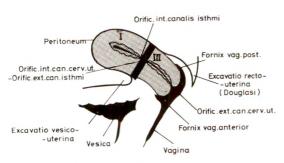


Fig. 1. Sketch showing the anatomic appearance of the isthmic canal area.

into the uterine cavity. The mandrin is withdrawn, a syringe is mounted, and 40 per cent urografin is injected into the balloon. The balloon head, which is thinner, expands first (Fig. 3). It is not until a certain amount of pressure is exerted upon the balloon head, as it fills the uterine cavity, that the neck expands, filling the isthmus and the cervical canal and thus clearly delineating the isthmic contour.

Since reflex spasm appears to occur in the isthmus in a number of cases, it is recommended that ample time be taken in expanding the balloon (10 to 15 minutes). It must also be realized that the pressure in the uterus may be fairly high, so that subjective complaints should be considered and the examination should not be forced if a great deal of sustained pain is present during the expansion of the balloon. For the same reason, this diagnostic method should only be used when there is clinical suspicion of habitual abortion. The balloon must be inspected under fluoroscopy so that the position of the head and neck of the balloon may be corrected, if necessary. We have

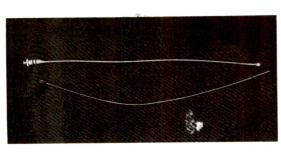


Fig. 2. Photograph of the balloon catheter with the mandrin withdrawn.

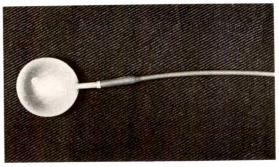


Fig. 3. Photograph of the balloon catheter expanded.

found that the pressure upon the uterine wall reaches a maximum of 150 mm. of mercury.

ROENTGEN FINDINGS

As already mentioned, the isthmus changes with the normal cyclic variations in the uterus. The maximum constriction is observed in the early secretory phase (16th–18th day), because at this time the tonus is most pronounced (Fig. 4). We have, therefore, performed our roentgenographic studies during this period, feeling that a diagnosis of possible isthmic incompetence would be most reliable during this

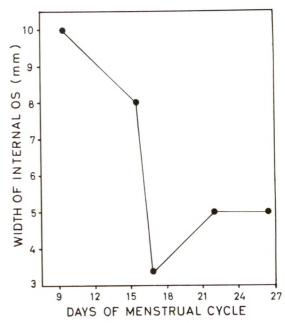


Fig. 4. Diagram showing the variations in isthmic width during the menstrual cycle.

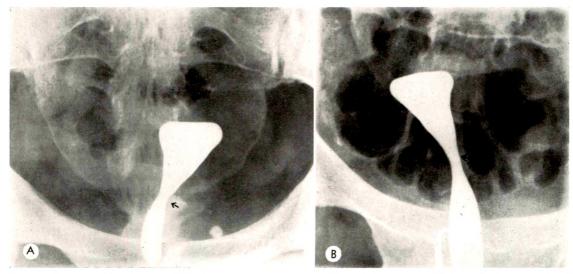


Fig. 5. (A and B) Hysterosalpingograms with balloon catheter in normal women on the 16th to 17th days of the menstrual cycle (in early secretory phase). Arrows indicate the sphincteric segment in the isthmic region.



phase of the cycle. Figure 5, \mathcal{A} and \mathcal{B} shows the appearance of the isthmus in normal women during this phase. A distinct, sphincteric segment in the isthmic region, normally 4 to 5 mm. in width, is demonstrated.

This technique for visualizing the isthmus has been of particular value in non-pregnant women, as the findings in such women presumably permit deductions concerning possible isthmic incompetence during pregnancy. Our series comprised only nonpregnant women.

The following cases are typical examples of patients in whom it was clinically felt that isthmic incompetence was responsible for habitual abortion.

ILLUSTRATIVE CASES

Case 1. This 30 year old woman had a history of 4 late miscarriages. During her last preg-

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Fig. 6. Thirty year old woman with a history of 4 late miscarriages. Hysterosalpingogram with the balloon catheter in early secretory phase shows isthmic hypotonia with dilated isthmic segment.

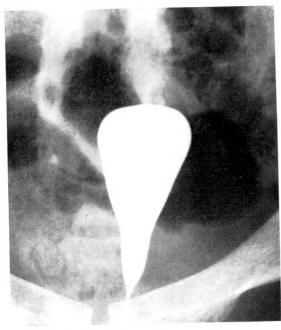


Fig. 7. Twenty-seven year old woman with a history of 3 miscarriages. Hysterosalpingogram with the balloon catheter in early secretory phase shows isthmic hypotonia with a dilated isthmic segment.

nancy, it had been suspected that isthmic incompetence might be responsible for her miscarriages. She was admitted with a threatened miscarriage in the 6th month of pregnancy. The typical syndrome of isthmic incompetence was present, characterized by painless, passive dilatation of the cervix, culminating in prolapse of the intact membranes and subsequent expulsion of the fetus. The patient was examined roentgenographically 6 months later in the early secretory phase of her menstrual cycle. Unlike the normal contracted isthmic segment, this patient showed isthmic hypotonia (Fig. 6), characterized by dilatation of the normally contracted isthmic segment. The patient was operated on employing the method of Shirodkar. She conceived soon after and was delivered, at calculated term by cesarean section, of a live girl weighing 3,500 gm.

Case II. This 27 year old woman had a history of 3 late miscarriages occurring in the 5th to 6th month. The clinical findings during her miscarriages were suggestive of isthmic incompetence. At a time when she was not pregnant, hysterography was performed using the balloon catheter. Isthmic hypotonia with a dilated isthmic segment, indicating sphincteric.

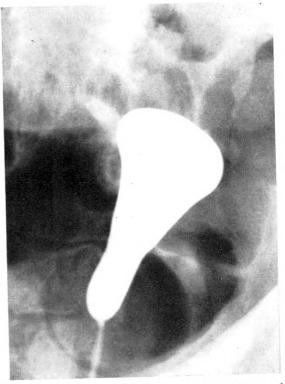


Fig. 8. Twenty-six year old woman with a history of 4 miscarriages. Hysterosalpingogram with the balloon catheter shows isthmic hypotonia with dilatation of the isthmic segment.

incompetence, was demonstrated (Fig. 7). In the 4th month of her next pregnancy, a Shirodkar operation was carried out. The patient was delivered spontaneously of a live girl, weighing 2,200 gm. a few weeks before the calculated term.

Case III. This 26 year old woman had a history of 4 miscarriages occurring in the 4th to 5th month. The clinical findings during her miscarriages suggested isthmic incompetence. Hysterography with the use of the balloon catheter, when she was not pregnant, showed isthmic hypotonia with dilatation of the normally contracted isthmic segment (Fig. 8). In the 3rd-4th month of her next pregnancy, a Shirodkar operation was done and the patient was delivered by cesarean section a short time before the calculated term of a live boy weighing 2,500 gm.

DISCUSSION

By hysterography employing a balloon catheter, the roentgenographic diagnosis of isthmic incompetence in nonpregnant women can be made. All of the cases described had clinical as well as roentgenographic changes indicating isthmic incompetence. The roentgenographic appearances were characteristic, showing dilatation of the normally sphincter-like segment, so that the isthmus and other parts of the cervix merged without any definite junction.

Several authors4 prefer operating when the patients are not pregnant. Our operations were performed using the method of Shirodkar, usually in the 3rd to 5th month of pregnancy. All 3 cases reported above had a history which was clinically suspicious of isthmic incompetence as responsible for the habitual abortions, and this suspicion was confirmed by roentgenography. After Shirodkar operations were carried out, all patients successfully completed their pregnancies. It is felt, therefore, that in cases where clinical examination leaves doubt, the diagnosis may be supported by hysterography using the balloon catheter.

SUMMARY

The technique of hysterography employing a balloon catheter for the visualization of the uterine isthmus is described. The advantage of using this catheter for hysterography is the possibility of diagnosing isthmic incompetence while the patient is

not pregnant and thereby establishing the probable cause of habitual abortion.

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HYSTEROSALPINGOGRAPHY WITH CONRAY 60 PER CENT AND A VACUUM UTERINE CANNULA

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THE purpose of this paper is to report the results of a hysterosalpingographic technique using conray 60 per cent as the contrast medium and a vacuum uterine cannula for leakproof adaptation to the cervix. This report is based on more than 200 hysterosalpingographic examinations.

There is still controversy about which of the contrast media is best for hysterosal-pingography; many authors use lipiodol, but most prefer water soluble contrast media. An ideal agent for hysterosalpingography should meet the following criteria: (1) be nonirritant and nontoxic; (2) be completely absorbed and excreted without damage to the area where it is introduced or to the organs from which it is excreted; (3) must not cause a foreign body reaction; (4) must be sufficiently radiopaque; and (5) must be fluid enough to pass easily through narrow channels, yet not reflux vaginally.

Lipiodol has some but not all of these properties. With lipiodol, there is danger of oil embolism when venous intravasation occurs. According to Grant, Callam and Davidson, 6 a total of 24 cases of pulmonary oil embolism during hysterosalpingography has been reported in the world literature since the condition was first described by Gajzago in 1931; in I case the embolism was fatal. Absorption of lipiodol is very slow and deposition in the peritoneal cavity can cause a foreign body reaction. The viscosity is high, although more fluid types of lipiodol are now used. The high viscosity creates difficulties in handling and injection; also, there may be penetration into tubes with reduced lumens and peritoneal spill (a 24 hour control may be necessary to demonstrate tubal patency).

Water soluble contrast media are preferable. There are no ill effects from venous

intravasations; they are absorbed rapidly and generally do not initiate a foreign body reaction. They pass rapidly into the peritoneal cavity, even when the tubes are narrow, and mix with fluid or secretion which is present in the uterus, tubes or peritoneal cavity. The disadvantages of the water soluble media are their low viscosity requiring a tight junction between the injecting cannula and the external cervical os: their relatively lower (but sufficient) radiopacity; and their rapid passage through the tubes, which sometimes leads to difficulty in demonstrating tubal morphology. These media may also cause complications such as low abdominal pain during and after the injection, chemical peritonitis, endometritis, and allergic phenomena. We have tried and abandoned endografin, which too frequently produces abdominal pain from peritoneal irritation for a period of 24 hours following the examination,3,9 and urografin which was found to be better.3,9,10 Water soluble contrast media thickened with substances such as polyvinyl alcohol, carboxymethyl cellulose, dextran, and tacholiquin have yielded improved but not ideal results.

MATERIAL AND METHOD

We have used conray 60 per cent as contrast medium for more than 200 hysterosal-pingographic examinations after abandoning angio-conray because of a high incidence of low abdominal pain during and after its instillation. With conray 60 per cent the frequency of abdominal pain was very low (only 36 patients). In some, a backache starting 3 to 4 hours after the examination lasted for almost 2 days. Neither the abdominal pain nor the back pain was severe enough to necessitate a

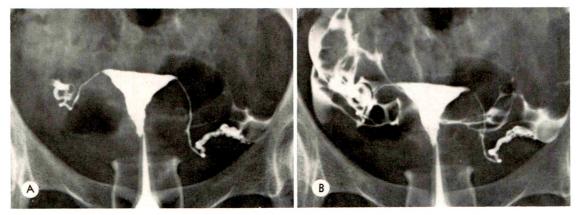


Fig. 1. Normal hysterosalpingograms. (A) After introduction of 4 cc. of conray 60 per cent. (B) After an additional 3 cc. of conray 60 per cent.

doctor's call. There were no significant allergic reactions; I patient had headache, nausea and vomiting starting within I hour after the examination and lasting for 2 days; 3 patients had slight fever associated with abdominal pain for I day after the

examination. With these exceptions, the examination produced no real discomfort or after effects.

The vacuum cannula provides very good fixation to the cervix and makes the procedure painless. The tight junction of the

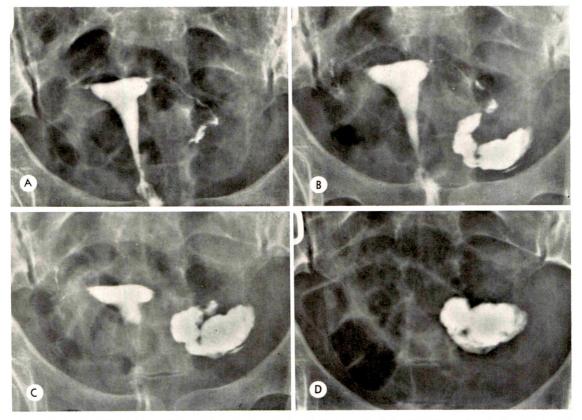


Fig. 2. (A and B) Occlusion of the right salpinx; hydrosalpinx on the left side. Retention is demonstrated on the (C) postvoiding roentgenogram and on the (D) control roentgenogram after 2 hours.

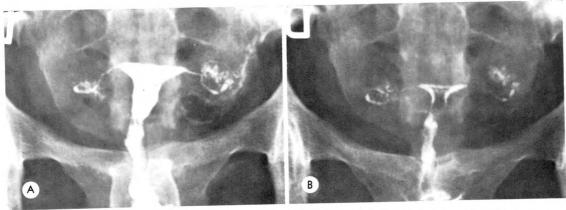


Fig. 3. (A and B) Tuberculous salpingitis. (B) The pathologic salpingitic pattern is evident in the postvoiding roentgenogram.

suction cup and cervix prevents leakage and allows the use of water soluble contrast media with low viscosity such as conray (6.1 cps at 25° C.). The cervix is gripped in a radiotransparent glass suction cup, the injection cannula with its acorn tip of rubber is introduced into the cervical os, and the vacuum presses the cervix down into the suction cup and forces the acorn upward, securing a tight fit between the cervical os and the surface of the rubber acorn. The injection cannula terminates in a piston in a metal cylinder. The cap is connected with an electric aspirator that produces a vacuum.

Most of the systems used for adaptation

of the cervical os with introduction of the cervical cannula require grasping of the cervix, and often the seal is incomplete. With the vacuum cannula, it is not necessary to use any tenacula; a vacuum of 0.4 kg./cm.² assures a perfect seal.⁴

After the insertion of a bivalve speculum, the cervix is exposed, the tip of the cannula is introduced into the cervical os and the vacuum is applied. The small tip of the cannula permits visualization of the entire cervical canal other than the uterus. The procedure is accomplished without discomfort. The speculum is removed and, under fluoroscopic control, 2 to 3 cc. of conray 60 per cent is introduced and the first spot

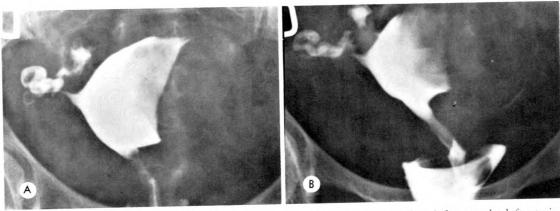


Fig. 4. (A and B) Large intramural myoma on the left side: large compression defect on the left uterine wall. (B) The postvoiding roentgenogram shows the appearance of the cervical canal and of the vagina which is slightly deviated to the right.

film is exposed. This film shows delineation of the cervical canal and uterine cavity. A second exposure is made after introduction of another 2 to 3 cc. of conray 60 per cent to visualize the tubes. A third exposure, always under fluoroscopic control, after introduction of another 2 to 3 cc. of contrast agent, demonstrates the peritoneal cavity if there is tubal patency. After the introduction of a penicillin solution, the suction device is removed and a last roentgenogram is made.

The contrast material in the peritoneal cavity is absorbed in 1 to 2 hours. A roentgenogram made after this time demonstrates its elimination through the urinary tract. This confirms, if necessary, tubal patency. Image intensified fluoroscopy is recommended to reduce radiation exposure. The tight seal afforded by the vacuum cannula permits useful maneuvers such as exerting traction on the cervix to visualize a markedly anteverted uterus and the turning of the patient for oblique and lateral exposures. The postvoiding roentgenogram is often useful for studying the mucosal pattern of the cervical canal and the uterine cavity. Figures 1 through 4 demonstrate the use of this technique.

CONCLUSION

- 1. Conray 60 per cent is not the ideal, but is the best available, contrast medium for hysterosalpingography.
- 2. The vacuum cannula is recommended for its complete sealing of the cervical os and less discomfort to the patient. Image intensification fluoroscopy should be used

to reduce the amount of radiation to the ovaries.

Via Costantinopoli, 84 Napoli, Italy

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E DITORIALS

THE PHENOMENON OF EXTRAVASATION AND ITS RELATION TO ACUTE URINARY OBSTRUCTION

THE phenomenon of extravasation during intravenous pyelography is, of course, a fortuitous visualization of a potential route for the escape of urine from the renal pelvis. This process is seen most frequently in states of acute urinary obstruction whether produced iatrogenically by compression, by calculus or by some other disease process.

The details of the pathophysiology of acute urinary obstruction differ among various authors. However, most authors describe a sharp rise in the intrapelvic pressure following acute obstruction. Despite this rise in pressure, the formation and secretion of urine continue. The exact role played by glomerular filtration and tubular secretion is unclear, and different emphasis is placed on each unit, depending on the author and his experience. 1,2 The continuous formation of urine despite obstruction of the normal route of excretion predicates compensatory resorption of urine. Numerous observations including those of Kiil3 indicate that the intrapelvic pressure following a period of acute obstruction is not significantly different from that of the normal pelvis. Various biochemical studies also reveal that urine within the obstructed pelvis is metabolically active. The route by which resorption occurs remained hypothetical until the phenomenon of extravasation during both retrograde and intravenous pyelography was described.

Available evidence suggests that the renal pelvis in a high percentage of cases

adapts to the rising pressure by a process of limited passive accommodation. The elastic tissue and smooth muscle allow the pelvis to expand to a limited extent in response to this stimulus.

The forniceal calyx, however, is involved much more intimately in the process of resorption. Again, the structure of the fornix allows some passive adaptation. The histologic studies of Narath¹ demonstrate that the undulating epithelium, the elastic lamina propria, and the loose adventitia allow some expansion under pressure. In addition, numerous radiographic observations reveal that the fornix is permeable to the passage of urine. Olsson4 felt that a small rupture occurs at this site and he is supported in this view by Harrow, 5 Ginsberg, 6 the contributors to this issue, and others. Contrariwise, Hinman⁷ and Narath¹ feel that the forniceal epithelium has resorptive capacities, citing failure to reproduce the phenomenon in subsequent retrograde and intravenous studies as evidence against actual rupture. In a current report, Schwartz et al.8 render an important contribution in their description of reproduction of extravasation in 4 of 16 patients.

Forsythe et al.9 and other investigators

6 GINSBERG, S. A. Spontaneous urinary extravasation in associ-

ation with renal colic. J. Urol., 1965, 94, 192-195.

 7 HINMAN, F., Jr. Peripelvic extravasation during intravenous urography: evidence for an additional route for backflow after ureteral obstruction. J. Urol., 1961, 85, 385–395.

8 SCHWARTZ, A., CAINE, M., HERMANN, G., and BITTERMANN, M. Spontaneous renal extravasation during intravenous urography. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1966, 98, 27–40.

⁹ Forsythe, W. E., Huffman, W. L., Schildt, P. J., and Persky, L. Spontaneous extravasation during urography. J Urol., 1958, 80, 393–398.

¹ Narath, P. A. Renal Pelvis and Ureter. Grune & Stratton Inc., New York, 1951. ² Hinman, F., Jr. The Pathology of Urinary Obstruction in:

Urology. Edited by M. Campbell. W. B. Saunders Co., Phila-

⁴ Olsson, O. Studies on back-flow in excretory urography. *Acta radiol.*, 1948, Suppl. 70.

⁵ Harrow, B. R. Spontaneous urinary extravasation associated with renal colic causing a perinephric abscess. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1966, 98, 47–53.

³ KIII., F. The Function of the Ureter and Renal Pelvis. W. B. Saunders Co., Philadelphia, 1957.

have reported studies which were interpreted as evidence of passage of urine from the fornix directly into the lymphatics of the renal sinus. The appearance of urine within the renal sinus was explained by rupture of these overburdened lymphatics. The current studies of Hinman⁷ and others indicate direct passage into the loose fatty and connective tissue of the renal sinus with subsequent absorption by lymphatic vessels.

From the renal sinus, fluid has several routes of egress. It has been clearly shown that a potential route exists between the renal sinus and the retroperitoneal space via the renal hilus. In addition, this has been observed innumerable times radiographically, and has not infrequently been misinterpreted. Resorption of urine via lymphatic vessels which originate in the renal sinus has been discussed above. Finally, a potential route exists for resorption via rupture or penetration of the pericalyceal venous plexus. Studies by Hinman and Lee-Brown¹⁰ have demonstrated a potential route between the renal pelvis and veins. However, Harrow⁵ has repeatedly criticized the evidence offered and points out the lack of in vivo evidence for this route of resorption.

Numerous investigators have suggested pyelotubular backflow as a further potential route of resorption. The appearance of opaque fluid in the collecting tubules in the acutely obstructed kidney has added further impetus to this concept. In an excellent paper, Fleischner *et al.*¹¹ postulate the slowed excretion of urine in the collecting tubules with subsequent resorption of water under the control of ADH as the reason for opacification of the tubules, and indeed, not reflux.

Various other forms of resorption have been advanced; however, data are lacking for their support.

The literature, as well as the excellent contributions made by our current authors, suggests that extravasation represents the compensatory resorption of urine in acute urinary obstruction, although this phenomenon is not frequently seen. There is no report in the English language literature to my knowledge of its incidence in acute obstruction. Numerous surgical reports, particularly in the urologic literature, describe edematous tissue and fluid in the retroperitoneal area about an acutely obstructed kidney. The impression contained therein suggests that extravasation is a common occurrence in this disease. Current opinion would then place radiographically visible extravasation as a fortuitous visualization of a basic homeostatic process in the acutely obstructed kidney.

Clinically, the extravasation, whether visualized or not, is usually benign, if the extravasated urine is sterile, if the obstruction is removed promptly, and if the possibility of a rent in the pelvis or ureter is successfully eliminated. However, if pyuria is present, perinephric and retroperitoneal abscess may be the sequela, as reported by Harrow.⁵ Furthermore, extravasation of sterile urine may evoke a retroperitoneal foreign body-like reaction which may then produce retroperitoneal fibrosis of the affected side with subsequent hydronephrosis as a late sequela.

All in all, it may be said that when extravasation is demonstrated, it is of the utmost importance for the radiologist and urologist to think of it in terms of the pathophysiology of acute urinary obstruction and, within limits, treat it with cautious observation.

Frederick R. Cushing, M.D.

Harper Hospital Detroit, Michigan 48201



¹⁰ Hinman, F., and Lee-Brown, R. K. Pyelovenous back-flow. *J.A.M.A.*, 1924, 82, 607–613.

¹¹ Fleischner, F., Bellman, S., and Henken, E. M. Papillary opacification in excretory urography. *Radiology*, 1960, 74, 567-572.



MARTIN SCHNEIDER, M.D. 1913-1966

DEATH came rather suddenly and unexpectedly to Martin Schneider on June 24, 1966. Although his friends and associates had noted a decline in vigor and strength for many months, Marty had continued to carry a full load of responsibility and had continued to see patients and direct the activities of the Radiotherapy

Department until within a few days of the end. One of his last acts before leaving his office to enter the hospital was to go over the records of all of his patients and leave directions for their care during his absence.

Dr. Schneider was born in New York City and attended elementary and high school in that city. He was graduated from the City College of New York in 1932 and then entered medical school at St. Louis University in St. Louis, graduating in 1936. He served his internship at the Queens General Hospital in Jamaica, New York, from 1936 to 1938. Following this, he took residency training at the Brooklyn Cancer Institute and Hines Hospital, Hines, Illinois. He became a diplomate of the American Board of Radiology in 1941, and shortly thereafter he joined the faculty of the University of Texas Medical Branch as a Research Associate in Radiology.

Immediately following the outbreak of the war in 1942, he entered active military service in the Air Force. He served until 1945 and was discharged with the rank of major. After his discharge, he returned to the University of Texas Medical Branch to become the Chairman of the Radiology Department which had just been placed on a full-time basis. He set about organizing various aspects of the training program for residents and improving the teaching of radiology in the medical school. While fully engaged in the many activities associated with the development of the department, he was in 1948 suddenly stricken with an attack of paralytic poliomyelitis. This was followed by a prolonged and trying period of convalescence, the final result being a complete diplegia. Within a year, however, he returned to work in a wheelchair, to which he was confined for the remainder of his life. Nevertheless, after a few months Marty made a complete readjustment and was soon able to return to a full-time career.

During the ensuing 18 years he served magnificently as a complete physician and academician. During this period he devoted his time almost exclusively to radiation therapy. By determined perseverance he was able to conduct every type of physical examination used in this specialty. Even in the operating room he was able to exert his judgment and influence and supervised his residents in radium applications. Also, as his strength increased he threw himself

increasingly into all of the varied activities of the medical school and the city of Galveston. He served on various committees of the faculty, was elected President of the local Sigma Xi Society and also served as the President of the Texas Radiological Society. He was active in the local Anti-Tuberculosis Association and the local chapter of the American Cancer Society. He was a Fellow of the American College of Radiology and a member of the American Roentgen Ray Society, the Radiological Society of North America, the International Congress of Radiation Research, and a member emeritus of the Association of University Radiologists. He regularly attended medical meetings and presented papers. Also, during this time he continued his interest in radiation biology. This is attested by the 45 publications comprising his bibliography, of which more than half are devoted to the fundamental effects of radiation on man and animals.

Despite his severe affliction, Marty was a happy and joyous person. Even under the most trying circumstances, it seemed that he could always come up with a witticism or observation that made things seem just a little bit easier. Many acquaintances looked forward to meeting him in the hallways of the hospital because of his cheery demeanor and trenchant comments, and doubtless these many pleasant attributes contributed considerably to his success in the handling of patients with cancer.

Dr. Schneider is survived by his wife, Rose G. Schneider, Ph.D., Research Associate Professor in the Department of Pediatrics at the University of Texas Medical Branch, by two daughters, Susan and Nancy, and a son, Stephen.

Marty will be sorely missed by his many friends, but doubtless the greatest loss will be to a host of appreciative patients, a number of whom owe their lives to his skill and perseverance.

ROBERT N. COOLEY, M.D.

Department of Radiology University of Texas Medical Branch Galveston, Texas

NEWS ITEMS

THE AMERICAN BOARD OF RADIOLOGY

The spring 1967 examination of The American Board of Radiology will be held at the Pittsburgh Hilton Hotel, Pittsburgh, Pennsylvania, June 5-9, inclusive. The deadline for filing applications for this examination is December 31, 1966.

The fall 1967 examination will be held at the Statler Hilton Hotel, Dallas, Texas, December 4–8, inclusive. The deadline for filing applications is June 30, 1967.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS

Annual Memorial Medal Award Competition

An annual Memorial Medal Award in honor of deceased AUR members is awarded to the resident in radiology writing the best original paper on some aspect of radiology during the period of competition. The paper must be the work of only one author, the resident. Manuscripts to be considered for the 1967 competition must be received by March 1, 1967. Inquiries should be addressed and papers submitted to the Secretary of the AUR, Dr. Stanley Rogoff, Department of Radiology, University of Rochester Medical School, Rochester, New York 14620.

The winner of the competition will be invited to present his work at the annual meeting of the Society which will be held on May 12 and 13, 1967 at Temple University School of Medicine, Philadelphia, Pennsylvania.

POSTGRADUATE COURSE ON RADIOLOGY OF CHEST DISEASES

Emory University

The Department of Radiology of Emory University School of Medicine will conduct a postgraduate course, Radiology of Chest Diseases, on October 28–29, 1966. This

course will be held at Grady Memorial Hospital, Atlanta, Georgia.

The guest faculty will be: Dr. Benjamin Felson, Cincinnati General Hospital; Dr. Robert G. Fraser, Royal Victoria Hospital, Montreal; Dr. James L. Quinn, III, Chicago Wesley Memorial Hospital; Dr. George Simon, St. Bartholomew's Hospital, London, England; and Dr. Leo G. Rigler, University of California, Los Angeles.

For further information, please write to H. S. Weens, M.D., Department of Radiology, Emory University School of Medicine, Atlanta, Georgia 30322.

WORKSHOP IN RADIOISOTOPE SCANNING

Emory University

The second Workshop in Radioisotope Scanning will be presented from October 23–27, 1966, immediately preceding the postgraduate course on Radiology of Chest Diseases to be held October 28–29, 1966.

The Workshop will consist of daily lectures, seminars, individual conferences, and practical exercises using a variety of scanning instruments and the scintillation camera. It is limited to individuals who have had previous experience with radioisotopes and who wish to add or extend scanning procedures to their diagnostic services.

The Guest Faculty participating in the Workshop includes: Dr. James Quinn of Chicago, Illinois; Dr. Douglas Ross and Mr. Craig Harris of Oak Ridge, Tennessee.

For further information, contact Joseph L. Izenstark, M.D., Division of Nuclear Medicine, Department of Radiology, Emory University School of Medicine, Atlanta, Georgia 30322.

ANNUAL PEDIATRIC POSTGRADUATE COURSE ON NEONATOLOGY

VARIETY CHILDREN'S HOSPITAL

The Variety Children's Hospital is presenting its Annual Pediatric Postgraduate

Course on *Neonatology* at the Deauville Hotel in Miami Beach, Florida, January 22–26, 1967.

An outstanding program has been arranged. The Guest Faculty comprises: Mary Ellen Avery, M.D., Baltimore, Maryland; William A. Cochrane, M.D., Halifax, Nova Scotia, Canada; Louis K. Diamond, M.D., Boston, Massachusetts; Heinz F. Eichenwald, M.D., Dallas, Texas; Sydney S. Gellis, M.D., Boston, Massachusetts; John A. Kirkpatrick, M.D., Philadelphia, Pennsylvania; Jerold F. Lucey, M.D., Burlington, Vermont; Edith L. Potter, M.D., Chicago, Illinois; Peter P. Rickham, M.D., Liverpool, England; and William A. Silverman, M.D., New York, New York.

For further information, please contact Dr. Donald H. Altman, Chairman of Postgraduate Course, Variety Children's Hospital, Miami, Florida 33155.

UROLOGICAL X-RAY CONFERENCE

A seminar dealing strictly with x-ray and its application to urology will be held under the auspices of the Division of Urology of the Department of Surgery of the Cincinnati General Hospital, at the Netherland Plaza Hotel, February 16 to 18, 1967.

For further information please contact Arthur T. Evans, M.D., Director, Division of Urology, Department of Surgery, Cincinnati General Hospital, University of Cincinnati College of Medicine, Cincinnati, Ohio 45229.

FIRST PAN AMERICAN CONGRESS OF ANGIOCARDIOGRAPHY

The Central-American Association of Radiologists and the Twelfth National Medical Congress of Medicine of Panama, will sponsor the First Pan American Congress of Angiocardiography to be held in Panama City, Republic of Panama, December 1–3, 1966.

Members of the Congress are those interested in roentgenographic diagnosis of cardiac and cardiovascular, congenital and acquired, lesions. Consequently, diseases of the pediatric group and adults will be equally considered as a matter of discussion and presentation. The subjects have been divided into 2 groups: (1) congenital diseases, and (2) acquired diseases. The latter comprises 3 subgroups: (a) rheumatic lesions, (b) atherosclerosis, and (c) infectious diseases (viral, bacterial, parasitic, etc.).

The Sessions of the Congress will be held at the Panama Hilton Hotel, where complete facilities are offered to all members attending the Congress. Scientific exhibits will be arranged and moving pictures will be shown.

Accommodations will be available at the Hotel Panama Hilton, Hotel Intercontinental, and Hotel Lux.

For reservations, write to Luis Arrieta, M.D., Executive Director, or to R. Avila, M.D., General Secretary of the Congress. Anyone wanting to participate in the scientific program should write to A. Castellanos, Sr., M.D., Variety Children's Hospital, 6125 S. W. 31st Street, Miami, Florida 33155.



BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

The Yearbook of Radiology (1965–1966). Radiologic Diagnosis edited by John F. Holt, M.D., Professor, Department of Radiology, University of Michigan, and Walter M. Whitehouse, M.D., Professor and Chairman, Department of Radiology, University of Michigan. Radiation Therapy edited by Howard B. Latourette, M.D., Professor, Department of Radiology, University of Iowa. Cloth. Pp. 478, with 344 illustrations. Price, \$12.00. Year Book Medical Publishers, Inc., Chicago, 1966.

Through the painstaking efforts of Drs. Holt, Whitehouse, and Latourette, we have been rewarded with one of the best Yearbooks of Radiology of a series that goes back many years. There seems to be no limit to the ingenuity of radiologic investigators and the vast outpouring of literature related to their field. Busy practitioners seldom have time to read all the material in their own specialty journals, let alone pertinent articles in foreign literature and in journals of related specialties. This Yearbook is, therefore, again recommended as enjoyable leisurely reading, as a handy reference source for problems in daily radiologic practice, and as a means of keeping abreast of the latest developments in the field.

For those unfamiliar with previous editions, the diagnostic section is replete with excellent reproductions of roentgenograms, charts and graphs, and the editors have punctuated most of the abstracts with pertinent editorial comment and cross references. The subjects dealt with range from the scintillation camera, computer analysis of radiologic images, and intensifier television systems to lymphangiography, visceral angiography, mammography, thermography and discussions of specific diseases. Dr. Holt has included many articles of interest in the field of pediatric radiology such as that dealing with transplacental rubella infection in newly born infants.

In the 172 pages devoted to therapy, Dr. Latourette has assembled an excellent group of articles on radiation effects and hazards, the biochemistry of cancer, combinations of treat-

ment modalities, and the newer sophisticated equipment and data processing facilities for use in our field. A special commendation is given to Dr. Gilbert Fletcher and his co-authors for the level of excellence of numerous articles included in this section.

The future indeed appears bright for both therapeutic and diagnostic radiology and tremendous advances appear certain within the next few years.

ARCH H. HALL, M.D.

Management of the Patient with Cancer. Edited by Thomas F. Nealon, Jr., M.D., Professor of Surgery, Jefferson Medical College. With contributions by seventy-one authorities. Cloth. Pp. 1067, with many illustrations. Price, \$27.50. W. B. Saunders Company, West Washington Square, Philadelphia, Pa., 1965.

To cover the entire field of cancer management in a single volume of slightly more than one thousand pages is indeed a formidable task.

Nonetheless, the editor appears to have achieved his stated objective: "to make available to the general practitioner, internist, and general surgeon the essential information concerning cancer of all sites in a sufficiently succinct manner that they can appreciate the best approach to the management of an individual." This has been accomplished by placing particular emphasis on signs and symptoms, diagnostic methods, selection of treatment modality, manifestations of recurrence, and end results.

The text, contributed by 71 authorities in the respective fields, is divided into two major sections. Part one, titled General Considerations, encompasses the principles of surgery, radiation therapy and chemotherapy. It also includes chapters on diagnostic techniques, history and physical examination, pathology and cancer research. Part two deals with cancer as it relates to the various anatomic sites, all of which are included.

The cancer specialist looking for detailed recommendations or in-depth discussion of areas of controversy will be disappointed. Even he, however, will find the extensive bibliography at the end of each chapter useful and rewarding.

HOWARD J. WEST, M.D.

BOOKS RECEIVED

RADIOLOGY OF THE TEETH AND JAWS: INCLUDING DENTAL RADIOGRAPHY; FOR STUDENTS AND PRAC-TITIONERS OF DENTAL SURGERY AND RADIOLOGY. By Frank L. Ingram, D.M.R.D., L.D.S., M.R.C.S., L.R.C.P., Consultant Radiologist to the Dental Department, Guy's Hospital, London, to the Eastman Dental Hospital, London, and to the Canterbury and Isle of Thanet Hospital Groups; Recognised Teacher of Dental Radiology at Guy's Hospital Medical School, in the Faculty of Medicine, London University; Lecturer to the Institute of Dental Surgery, Eastman Dental Hospital; Past President of the British Society of Dental Radiology. Cloth. Pp. 256, with 394 illustrations. Price, \$11.75. The Williams & Wilkins Company, Baltimore 2, Md., 1966.

THE YEAR BOOK OF NUCLEAR MEDICINE. Volume 1—1966. Edited by James L. Quinn, III, M.D., Assistant Professor of Radiology, Northwestern University; Director of Nuclear Medicine, Chicago Wesley Memorial Hospital; Consultant in Nuclear Medicine, Veterans Administration Research Hospital, Chicago and Great Lakes Naval Hospital, Great Lakes, Ill. Cloth. Pp. 384, with 105 illustrations. Price, \$10.00. Year Book Medical Publishers, Inc., 35 E. Wacker Drive, Chicago, Ill., 1966.

RENAL ANGIOGRAPHY. Edited by Owings W. Kincaid, M.D., Section of Radiology, Mayo Clinic; Assistant Professor of Radiology, Mayo Graduate School of Medicine (University of Minnesota), Rochester, Minn.; Assistant Editor, George D. Davis, M.D., Section of Radiology, Mayo Clinic; Assistant Professor of Radiology, Mayo Graduate School of Medicine (University of Minnesota), Rochester, Minn. Cloth. Pp. 275, with 226 illustrations. Price, \$16.00. Year Book Medical Publishers, Inc., 35 E. Wacker Drive, Chicago, Ill., 1966.

RADIATION PROTECTION IN EDUCATIONAL INSTITU-TIONS, Recommendations of the National Council on Radiation Protection and Measurements. NCRP Report No. 32. Paper. Pp. 57, with some charts. Price, \$0.75. NCRP Publications, P. O. Box 4867, Washington, D. C. 1966.

ARTERIOGRAPHY: PRINCIPLES AND TECHNIQUES; EMPHASIZING ITS APPLICATION IN COMMUNITY HOSPITAL PRACTICE. By Joseph L. Curry, M.D., and Willard J. Howland, M.D., Department of Radiology, Ohio Valley General Hospital, Wheeling, W. Va. Cloth. Pp. 328, with 223 illustrations. Price, \$14.00. W. B. Saunders Company, West Washington Square, Philadelphia, Pa., 1966.

THE FIRST FIFTY YEARS; RADIUMHEMMET 1910-

1937 AND KING GUSTAF V JUBILEE CLINIC 1938–1960. By Elis Berven, Sven Hultberg, Hans-Ludvig Kottmeier, Rolf Sievert, Lars Santesson, and Bengt Sylvén. Paper. Pp. 200, with many illustrations. Acta Radiologica, Supplementum 250. Acta Radiologica, Stockholm 2, Sweden, 1965.

TREATMENT OF LEGG-CALVÉ-PERTHES DISEASE:
ASSESSMENT OF THERAPEUTIC RESULTS WITH
PARTICULAR REFERENCE TO THE VALUE OF TRACTION IN BED. By Johannes Meyer. Paper. Pp. 111,
with some illustrations. Acta Orthopaedica Scandinavica, Supplementum No. 86. Munksgaard,
Copenhagen, 1966.

STUDIES ON THE HAND IN ULNAR NERVE PARALYSIS:
A CLINICAL-EXPERIMENTAL INVESTIGATION IN
NORMAL AND ANOMALOUS INNERVATION. By
Lennart Mannerfelt. Paper. Pp. 176, with many
illustrations. Acta Orthopaedica Scandinavica,
Supplementum No. 87. Munksgaard, Copenhagen,
1966.

Forces Acting on the Femoral Head-Prosthesis: A Study on Strain Gauge Supplied Prostheses in Living Persons. By Nils W. Rydell. Paper. Pp. 132, with some illustrations. Acta Orthopaedica Scandinavica, Supplementum No. 88, ad Volumen 37. Munksgaard, Copenhagen, 1966.

L'Ostéochondrose Synoviale: Ostéochondromatose d'Henderson. By M. de Pontville, Chef de Clinique d'Électro-Radiologie; Assistant des Hôpitaux de Dijon; C. Perreau, Membre de la Ligue Française contre le Rhumatisme; F. Cabanne, Directeur de l'Ecole Nationale de Médecine et de Pharmacie de Dijon, Professeur d'Anatomie Pathologique; and G. Piganiol, Professeur Agrégé Chirurgien des Hôpitaux de Dijon. Paper. Pp. 132, with 62 figures. Price, 34F. Masson & Cie, Editeurs, 120, Boulevard Saint-Germain, Paris, 1066.

RADIOACTIVE PHARMACEUTICALS. Proceedings of a symposium held at the Oak Ridge Institute of Nuclear Studies, an operating unit of Oak Ridge Associated Universities, November 1–4, 1965. Edited by Gould A. Andrews, M.D., Ralph M. Kniseley, M.D., Henry N. Wagner, Jr., M.D., and Technical Editor, Elizabeth B. Anderson, M.S. Paper. Pp. 728, with some illustrations. Price, \$5.00. U. S. Atomic Energy Commission: Division of Technical Information. Available as CONF-651111 from Clearinghouse for Federal Scientific and Technical Information, National Bureau of Standards, U. S. Department of Commerce, Springfield, Va., 1966.

THE TREATMENT OF FRACTURES. By Lorenz Böhler, M.D., Director of the Accident Hospital, Vienna XX; Professor of Accident Surgery, University of Vienna. Supplementary Volume to the 5th English Edition by Prof. Dr. Lorenz Böhler, and Prof. Dr. Jörg Böhler. Cloth. Pp. 403, with many illustrations. Price, \$28.75. Grune & Stratton, Inc., 381 Park Avenue South, New York, N. Y., 1966.

ABSTRACTS OF RADIOLOGICAL LITERATURE

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ROENTGEN DIAGNOSIS Head

Rowley, John C., and Holmes, R. Brian. Sinus of Valsalva aneurysms. J. Canad. A. Radiologists, Dec., 1965, 16, 254–261. (From: Toronto General Hospital, Toronto, Ontario, Canada.)

Ruptured and unruptured aneurysms of the aortic sinuses are being encountered with increasing frequency since the development of cardiac catheterization and angiography. There are 2 types of aneurysms: acquired and congenital. Acquired aneurysms may be due to syphilitic aortitis, bacterial endocarditis, dissection and atheromatous degeneration of the aortic root. These tend to rupture outside of the heart. Congenital aneurysms of the sinus of Valsalva, on the other hand, arise from the right or noncoronary sinuses in over 95 per cent of the cases and tend to rupture into a right heart chamber usually during the fourth decade of life. Both types of aneurysms are usually asymptomatic until rupture occurs.

The authors give an anatomic classification of congenital aortic sinus aneurysms and briefly discuss the various theories regarding the etiology and pathogenesis of this anomaly.

In unruptured aneurysms the roentgenographic findings are usually normal. In I case curvilinear calcification in the wall of the aneurysm was noted.

After rupture, the findings depend on the magnitude of the shunt. In all of these cases enlargement of the right atrium and ventricle was present in association with pulmonary plethora of variable degree.

Contrast studies demonstrate the aneurysm and usually show a jet of contrast material passing into a right heart chamber. Early opacification of the pulmonary artery is confirmatory evidence of the shunt. —Francis P. Shea, M.D.

Moss, Arthur J., and Bruhn, Fred. The echocardiogram: an ultrasound technic for the detection of pericardial effusion. New England J. Med., Feb. 17, 1966, 274, 380–384. (From: Cardiopulmonary Unit, Department of Medicine, University of Rochester School of Medicine and Dentistry, and Medical Clinics, Strong Memorial Hospital, Rochester, N. Y.)

Utilizing the Ekoline 20 Diagnostic Ultrasonoscope, echocardiograms were obtained in 35 control subjects and 8 patients with clinically suspected pericardial effusion.

In the control group 33 subjects had a single echo recording from the posterior ventricular wall. There were 2 subjects in whom the posterior wall echocardiogram could not be obtained. One subject was extremely obese and the other had chronic pulmonary disease with emphysema.

In all 8 patients with suspected pericardial effusion a double posterior surface echo was obtained. The presence of the effusions was confirmed in 5 patients by a positive carbon dioxide study, in 1 patient by angiocardiography and in 1 patient by special roent-genographic studies. In the 1 false positive, a small effusion may have been missed since the carbon dioxide studies are done in the left lateral decubitus position and small amounts of fluid may gravitate away from the right atrium. The echocardiogram is performed in the supine position and fluid gravitates posteriorly.

From this study the authors conclude that the echocardiogram appears to be a simple innocuous and relatively accurate clinical technique for the detection of pericardial effusion.—Forrest Arnoldi, M.D.

KLEINFELD, MORRIS. Pleural calcification as a sign of silicatosis. Am. J. M. Sc., Feb., 1966, 251, 215–224. (From: State University of New York, Downstate Medical Center, Brooklyn, N. Y.)

Pleural calcification has been observed in about 0.15 to 0.20 per cent of chest roentgenograms. Tuberculous pleurisy, empyema, and traumatic hemothorax are common causes of this condition. Of the agents capable of producing a pneumoconiosis, only asbestos, talc, and mica, and rarely free silica have been incriminated in the production of pleural calcifications. In a series of roentgenograms of large groups mining coal, copper, iron, chrome, and manganese in two districts of South Africa, not a single case of pleural calcification was found.

The author reports 8 cases showing various degrees of pleural calcification from exposure to talc, asbestos, or mica. The minimum duration of exposure was 23 years and the maximum 54 years.

In addition to pleural calcification, the chest roentgenograms also showed varying degrees of pulmonary fibrosis in 5 instances. Also, in 5 cases the calcification was confined to the diaphragmatic region. Respiratory symptoms were present in 6 of the 8 cases, and pulmonary function studies were abnormal in 4.—James R. Knapp, M.D.

ABDOMEN

Parfitt, A. M. Familial neonatal hypoproteinaemia with exudative enteropathy and intestinal lymphangiectasis. *Arch. Dis. Childhood*, Feb., 1966, 41, 54–62. (From: Medical Unit, University College Hospital, London, England.)

In this article the author reports reinvestigation findings in a child with neonatal edema who was previously reported in the literature as a case of idiopathic hypoproteinemia. He shows that the patient has protein-losing enteropathy and steatorrhea as well as an abnormal small bowel histology with

dilated lymphatic spaces and partial villous atrophy. In addition, he reports that the patient's symptom-free sister also has protein-losing enteropathy.

Hypoproteinemia and edema are usually found in association with cirrhosis of the liver or the nephrotic syndrome. However, when these and other less common conditions are excluded, there remains a group of patients labelled "idiopathic hypoproteinemia." Increased catabolism of albumin in these cases has been demonstrated by several methods. Noteworthy among these has been demonstration of the gastrointestinal tract as the site of increased catabolism of albumin. This was first made on a patient with Menetrier's disease or giant rugal hypertrophy of the stomach. Later, Gordon (1959) introduced I131_ labelled polyvinyl pyrrolidone (PVP) and Waldman (1961) Cr51-labelled albumin. These substances readily demonstrated the increased loss of protein into the gastrointestinal tract in patients with idiopathic hypoproteinemia. The term "protein-losing enteropathy" (PLE) therefore simply means an increased leak of protein into the gut and may be a manifestation of many different diseases. However, PLE may occur without any demonstrable abnormality of the small bowel wall. Interestingly, although patients with idiopathic hypoproteinemia and PLE may have no overt evidence of intestinal disease, it has been shown that many of them have a structural abnormality of the small bowel wall most easily demonstrated by electron microscopy. This is characterized chiefly by dilatation of small lymphatics (intestinal lymphangiectasis).

Roentgenographically, the barium meal examination shows evidence of mucosal thickening in the small intestine and abnormal flocculation of the contrast material.

The author reviews the literature on PLE and reports published records of 49 cases in which hypoproteinemia and edema had begun in childhood. He emphasizes the association of PLE with steatorrhea in many patients. In some of these there is a recognizable lesion found in the small bowel, such as lymphangiectasis, Crohn's disease, granulomatous jejunitis, jejunal diverticulitis or villous atrophy of sprue. In other cases in which the association has been found the small bowel is apparently normal but there is some predisposing or associated condition such as gastroenteritis, postgastrectomy syndrome or carcinoma of the bronchus.—Lionel W. Young, M.D.

Graham, John R., Suby, Howard I., Le-Compte, Philip R., and Sadowsky, Norman L. Fibrotic disorders associated with methysergide therapy for headache. *New England J. Med.*, Feb. 17, 1966, 274, 359–368. (Address: Dr. Graham, Chief, Medical Service, Faulkner Hospital, Boston, Mass.)

The authors reviewed 27 cases of retroperitoneal fibrosis which developed during methysergide treat-

ment for headaches. Fourteen cases were treated surgically and 13 treated by withdrawal of the drug.

It was found that the exacerbations and remissions of the disease went hand in hand with the methysergide therapy. Thus, they recommend, that in cases of retroperitoneal fibrosis in patients on methysergide therapy, cessation of the drug be tried prior to surgical exploration.

Pathologically, the biopsied tissues in patients on methysergide therapy were similar to those reported in "idiopathic" cases.

From their findings the authors present evidence suggesting a possible relationship of methysergide therapy to fibrosis of the aorta, heart valves and pulmonary tissue, although they state that further observations are necessary for confirmation of these findings.

There is also a possibility that methysergide may precipitate changes in patients who are predisposed to collagen disorders.—Forrest Arnoldi, M.D.

Fass, Leroy, Anderson, Fred W., and Young, Lawrence E. Delay in diagnosis of carcinoma of right side of colon in patients treated for anemia. Am. J. M. Sc., March, 1966, 251, 255–259. (From: Department of Medicine, University of Rochester School of Medicine and Dentistry and Medical Service, Strong Memorial Hospital and the Genesee Hospital, Rochester, N. Y.)

Although experience has shown that anemia is a common sign of carcinoma of the right side of the colon, treatment of this early sign by self medication or by professional help frequently is made without adequate search for its cause.

This study was undertaken to discover the frequency with which patients are treated for periods of 30 days or more prior to definitive diagnosis. Records of 303 cases of carcinoma of the right side of the colon were reviewed. Twenty per cent were found to have been treated for anemia prior to diagnosis. Twelve per cent were treated for anemia without proper diagnostic evaluation for periods ranging from 1 month to 3 years.

It was found that physicians were relatively diligent in investigating patients with symptoms related to the gastrointestinal tract but less diligent in investigating patients with anorexia, weight loss, fatigue, and symptoms possibly related to anemia.— David C. Alftine, M.D.

Kraft, Ernest, Finby, Nathaniel, Egidio, Paul T., and Glenn, James S. The megasigmoid syndrome in psychotic patients. J.A.M.A., March 28, 1966, 195, 1099–1101. (Address: Dr. Kraft, Veterans Administration Hospital, Northport, N. Y.)

Psychotic patients frequently have unusual and bizarre gastrointestinal roentgenographic patterns.

The megasigmoid syndrome signifies a chronic bowel enlargement which is confined to the rectosigmoid. At times, pronounced enlargement of the rectosigmoid is observed with crowding of all abdominal organs upward to the chest. Great accumulations of fecal material occur making the digital removal of these masses imperative.

Complications comprise perforation of stercoraceous ulcers.

Long term psychotic patients are predominantly affected because they are more prone to develop organic brain changes.—David C. Alftine, M.D.

GARDNER, A. M. N., HOLDEN, W. S., and MONKS, P. J. W. Disappearing gall-stones. *Brit J. Surg.*, Feb., 1966, 53, 114–120. (From: Departments of Surgery and Radiology, Torbay Hospital, England.)

Seven cases of disappearing gallstones are reported and 15 previously reported cases are reviewed.

These cases are most common in females, particularly below the age of 30 years. Seven of the total 22 cases showed some relationship to pregnancy.

Although most patients have biliary colic, spontaneous passage may occur without pain and without clinical jaundice. This spontaneous passage may sometimes explain the situation where a clinician is faced with a case of typical biliary colic and then finds a normal gallbladder on subsequent cholecystography.—Alan G. Greene, M.D.

HERMANN, ROBERT E. Operative cholangiography. *GP*, March, 1966, 33, 120–127. (From: Cleveland Clinic, Cleveland, Ohio.)

Operative cholangiograms allow the identification of stones or other lesions in surgically hazardous or obscure areas. When performed carefully, operative cholangiography has proved to be absolutely safe. At the Cleveland Clinic the procedure is employed routinely, and it is believed that is is most valuable when used in this manner.

The value of operative cholangiography as a routine procedure is four-fold: (a) it helps the surgical team develop increased accuracy, proficiency and speed; (b) it precludes unnecessary common bile duct exploration when the operative cholangiogram is normal; (c) it demonstrates unsuspected stones in otherwise "normal" common bile ducts; and (d) it achieves safe visualization of hidden areas or those known to be surgically hazardous.

Operative cholangiograms may be obtained by any of 4 methods with equal facility and accuracy: (1) through the intact gallbladder; (2) through the partially divided cystic duct; (3) by direct puncture of the common bile duct; and (4) by needle puncture through the liver into the intrahepatic biliary system.

1. The first method is used when the gallbladder and bile ducts appear normal (as in patients with

hepatitis or recurrent pancreatitis); when the patient has obstructive jaundice due to an inoperable carcinoma of the pancreas and the gallbladder may be used in a biliary bypass procedure; or when a newborn infant has jaundice and it is necessary to determine whether biliary atresia is present.

2. When cholecystectomy is to be performed, the simplest method of obtaining an operative cholangiogram is via the cystic duct.

3. The third method, by direct puncture of the common bile duct, is used when the gallbladder has been removed previously.

4. The final method, by needle puncture of the dilated intrahepatic biliary system through the liver, is of most value in difficult re-explorations of the biliary system for jaundice, when after previous surgery the structures of the right upper quadrant may be distorted. This method of transhepatic cholangiography may be carried out either immediately before the abdomen is opened (percutaneous) or during the operative procedure.

The author states that this visual evidence of hidden stones or unexpected pathologic change has been far more accurate than the indirect indications formerly relied on by many surgeons as guides to the need for common bile duct exploration. In his last 200 patients on whom routine operative cholangiographies have been performed, unsuspected stones were found in 12—an incidence of 6 per cent. In these patients, no finding other than the operative cholangiogram indicated that a stone was present in the common bile duct. After open surgical exploration of the common bile duct with removal of stones, a second operative cholangiogram is always obtained before closing the abdomen. On at least 3 occasions a stone was found that had been overlooked in spite of careful manual exploration of the common bile duct.

Techniques of carrying out the various methods of operative cholangiography are discussed in detail.—
Douglas S. Kellogg, M.D.

BERK, J. EDWARD. Visualization of the bile ducts and portal venous system. J.A.M.A., March 21, 1966, 195, 1020–1024. (Address: 1721 Griffin Avenue, Los Angeles, Calif. 90031.)

The major methods currently employed to visualize the bile ducts are cholangiography with oral or intravenous administration of contrast medium, transhepatic cholangiography with percutaneous administration of the contrast material, and peritoneoscopic and operative cholangiography.

With oral cholangiography, calcium ipodate is quickly absorbed from the gut, promptly removed from the blood by the liver, and excreted into the bile. This makes it possible to visualize the bile ducts within 1 to 3 hours following its ingestion.

Comparative studies, however, indicate that cholangiography with oral administration of calcium

ipodate is in general less effective than with intravenous administration of the contrast medium, both as regards the frequency of visualization and the degree of opacification of the common bile duct.

Another noteworthy development is the use of intravenously administered cholecystokinin as an adjunct to cholecystography. This hormonal preparation causes rapid contraction of the gallbladder and simultaneous relaxation of the choledochal sphincter. With this method the cystic and common bile ducts may be visualized within I minute and maximally opacified within Io minutes after the intravenous injection of cholecystokinin and pancreozymin.

In percutaneous transhepatic cholangiography a needle-catheter assembly is inserted into the liver, and then slowly withdrawn until bile is aspirated. After more bile is gently aspirated, the contrast material is injected. Although the success rate with percutaneous transhepatic cholangiography is gratifyingly high, approximately 10 per cent of cases of established obstructive jaundice do not produce a successful cholangiogram. The most dreaded complication of the procedure is choleperitoneum, this complication having been reported in approximately 3 per cent of the cases. The author states that it is his policy not to employ transhepatic cholangiography unless it has been pre-arranged for operation to be carried out within a maximum of 4 to 6 hours after the cholangiographic examination when the latter reveals the existence of extrahepatic obstruction.

Peritoneoscopic cholangiography has never been widely adopted in the United States. Its greater value is probably in the jaundiced patient whose gallbladder is intact. Even in these cases, percutaneous transhepatic cholangiography would likely be the preferred procedure.

Cholangiography performed on the operating table to determine principally whether surgical exploration of the bile ducts is necessary is being increasingly employed. Wider use of this procedure has been aided by improved techniques for its performance and by the development of newer filming materials.

In percutaneous transhepatic portovenography, a major branch of the portal vein may be entered by inserting a long needle through a point in the middle just below the xiphoid process, and contrast material rapidly injected. Portovenography via a tributary vein may be accomplished by the technique of splenic portography, with the contrast material being injected into the splenic pulp. Another method of visualizing the portal system is by instillation of opaque material into a catheter inserted into the umbilical vein. In some cases it may be accomplished by injection of contrast medium into a hemorrhoidal vein. Retrograde hepatic venography, arteriovenography, and venography via the inferior vena cava after portacaval shunt are also discussed.

Techniques of the various methods are described in detail.—Douglas S. Kellogg, M.D.

GENITOURINARY SYSTEM

SMITH, IRVINE. Urography during renal colic. Brit. J. Surg., Feb., 1966, 53, 93-102. (From: General Hospital, Burton upon Trent, Staffordshire, England.)

The author describes the results of 50 urographic examinations performed during the course of acute renal colic for the diagnosis of acute obstruction, primarily due to calculus.

The characteristic signs of delayed excretion, enlarged nephrogram and slow filling of the dilated collecting system are discussed. In 86 per cent of the cases, delayed roentgenographic study enabled the identification of the cause of obstruction. Some of the delayed studies had to be extended up to 24 hours.

During renal colic, 27 kidneys were significantly larger than their normal size with a mean difference of 1.23 cm. (F.E. = 0.35; P greater than 0.001). In one-third of 38 kidneys, comparison with the opposite side was misleading because of previous disease.

The author advocates the use of urography during the acute colic phase as a means of demonstrating in a high percentage of cases the site and cause of obstruction. In addition, the procedure excludes those cases with similar clinical symptoms as well as the occasional malingerer.—Donald S. Linton, Fr., M.D.

EL-BADAWI, A. A. Bilharzial polypi of the urinary bladder. *Brit. J. Urol.*, Feb., 1966, 38, 24-35. (From: Faculty of Medicine, University of Alexandria, Alexandria, U. A. R.)

The author describes the bilharzial masses of the urinary bladder and divides them into three types. They are as follows: granulomatous polyp, fibrocalcific polyp, and villous polyp.

The microscopic and physical findings are described. The patients' symptoms are also tabulated.

The findings on plain roentgenograms as well as excretory urograms are well documented. Several reproductions of roentgenograms are included.

This report is based upon the study of 86 cases.— David C. Alftine, M.D.

Newsam, J. E., and Tulloch, W. Selby. Metastatic tumours in the kidney. *Brit. J. Urol.*, Feb., 1966, 38, 1-6. (From: Western General Hospital, Edinburgh, Scotland.)

Metastatic malignant disease of the kidneys rarely generates great clinical interest because it is often silent, and, more importantly, attention is focused on the primary site or those areas of metastasis which are highly symptomatic.

The authors report a series of 13 adult patients with primary carcinoma of the lung and renal metastases. The diagnosis of primary bronchogenic carcinoma was established ante mortem in 12 of the patients. A single patient had an occult primary ade-

nocarcinoma of the lung discovered at autopsy. Ten patients had a lobectomy or pneumonectomy in an attempt to cure the primary disease.

The antemortem clinical picture of renal metastatic disease was that of flank or abdominal pain associated with hematuria. In an attempt to control these symptoms, nephrectomy was performed in 9 patients, and exploratory laparotomy in a single patient. The remainder of the renal metastases were diagnosed by roentgenographic means, and surgery was not attempted.

The authors conclude, drawing heavily on the work of previous investigators, that the commonest malignant tumor of the kidney is metastatic from primary bronchogenic carcinoma. They find that this site of metastasis, while being frequently silent, can present a recognizable clinical entity requiring at times vigorous therapy for control of symptoms.—

Frederick R. Cushing, M.D.

Porstmann, W., Wierny, L., and Münster, W. Die selektive Nebennierenangiographie. (Selective adrenal angiography.) Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin, Feb., 1966, 104, 150–157. (From: Abteilung für kardiovaskuläre Diagnostik der Medizinischen Fakultät [Charité], Schumannstr. 21–20, Berlin N. 4, Germany.)

The adrenals are highly vascularized but their angiographic visualization is rarely satisfactory because the numerous arteries are very narrow. Regular superior, middle and inferior adrenal arteries are infrequently encountered, since they may variably originate in the phrenic artery, the celiac axis, the renal, superior mesenteric and spermatic arteries, also in accessory renal arteries and in vessels branching to the renal capsule.

In order to improve the visualization of the adrenals, the authors use selective angiography after having predetermined from aortography which arteries are most suitable for introduction of a catheter. They inject 4 to 6 ml. of a 60 per cent solution of diatrizoate contrast material (Visotrast, Uromiro, Urografin). Six exposures per second are made for the first 3 seconds, to be followed by 2 to 3 exposures at 5 second intervals. With this technique, small tumors can be well demarcated from normal tissues and from extrinsic masses hugging the adrenal.

The method was used in 4 patients with pheochromocytoma and in 1 with a small adenoma. In 2 additional patients, the findings were normal. Angiographic signs of tumors are as follows: pathologic vessels, arteriovenous fistulae, lacunae, premature venous drainage, displacement of vessels, tumor staining and avascular areas. No complications were encountered, and an indication for selective angiography always existed when aortographic findings were suggestive of a tumor.—Ernest Kraft, M.D.

SKELETAL SYSTEM

PIRKER, E. Ein röntgenologischer Beitrag zur Pathogenese des Syndroms von Klippel-Trenaunay. (Roentgenologic contribution to the pathogenesis of the Klippel-Trenaunay syndrome.) Radiol. Austriaca, 1966, 15, 243—248. (From: Zentral-Röntgeninstitut und Radiologische Universitätsklinik, Graz, Austria.)

The Klippel-Trenaunay syndrome presents with partial gigantism of an extremity (most frequently a lower extremity). It is a congenital angio-osteohypertrophy of unknown etiology. The following vascular changes are encountered: angioma of the skin, varices, and arteriovenous fistulae. There are vascular changes in the bones and in the surrounding soft tissues and a systemic circulatory disturbance with cardiac enlargement.

The case of a 7 year old girl is reported in whom the right lower extremity was involved. The leg was increased in length and thickness. Minute lymph cysts were present throughout the skin. The heart was enlarged to the left and right. Angiography revealed presence of arteriovenous fistulae and an early venous phase, but no varices. Lymphangiography disclosed innumerable minute lymphatic cysts but no regular lymphatic channels.

The author believes that the arteriovenous fistulae are the most important factor in causing hyperemia and stimulation of increased growth with hypoxia of tissues. Careful angiographic studies are advocated in patients with overgrowth of a single extremity to determine presence or absence of arteriovenous fistulae which are so characteristic of the Klippel-Trenaunay syndrome.—Ernest Kraft, M.D.

CRABBE, W. A. Intra-osseous ganglia of bone. Brit. J. Surg., Jan., 1966, 53, 15-17. (From: Guy's Hospital, London, England.)

This is a report of 10 cases with isolated cystic lesions in the epiphyseal region of long bones or the carpal or tarsal bones.

The cysts lie in the subchondral region; the margins are sclerotic. There is no expansion of the bone. There may be degenerative changes in the adjacent joint which apparently are coincidental. The tibia is involved most frequently.

Macroscopically, the cysts contain a clear gelatinous fluid and have a firm fibrous wall which is no more than a few cells thick. The author regards these lesions as intra-osseous ganglia in view of the very close macroscopic and histologic similarity to a soft-tissue ganglion. He differentiates them radiologically from osteoarthritic and rheumatoid cysts since they are usually larger, solitary and have a sclerotic margin.

One cyst recurred after curettage and then was

excised. Nine other patients were relieved of aching pain by curettage.—Martha Mottram, M.D.

SHEA, DARRYL, and MANKIN, HENRY J. Slipped capital femoral epiphysis in renal rickets: report of three cases. J. Bone & Joint Surg., March, 1966, 48-A, 349-355. (From: Department of Orthopaedic Surgery, University of Pittsburgh, Pittsburgh, Pa.)

Three cases of slipped capital femoral epiphysis associated with renal rickets are reported. Possible etiologic causes, such as a defect in protein synthesis, and hormone imbalance are discussed.

In all 3 cases, because of the hazard of a surgical procedure in patients with anemia, hypertension, bleeding tendencies and electrolyte abnormalities, treatment was conservative with partial or complete non-weight-bearing. No progression or increased disability was noted.

On the basis of their experience, the authors suggest that this may indeed be the preferred treatment for epiphyseolysis in chronic renal failure.—Alan G. Greene, M.D.

Frantz, Charles H., and Delgado, Sergio. Limb-length discrepancy after third-degree burns about the foot and ankle: report of four cases. J. Bone & Joint Surg., April, 1966, 48-A, 443-450. (Address: 313 Blodgett Medical Building, Grand Rapids, Mich.)

Four cases of severe burns of the lower limbs in children, with follow-up of 7-15 years are reported. Growth retardation resulting in limb length discrepancy after third-degree burns about the foot and ankle is discussed.

The precise mechanism causing growth retardation in severely burned extremities is not well understood. Impairment of epiphyseal growth which might result from prolonged ischemia of the epiphyseal plate is mentioned. (In this connection, it has been demonstrated that epiphyseal cartilage is much more sensitive to x-rays than articular cartilage.)

In 2 of the cases, there was premature closure of the distal tibial epiphyseal plate and associated spontaneous fusion of the ankle joint, probably resulting from the initial thermal damage to the epiphyseal plate. In the remaining 2 cases, despite severe burns, premature closure of the epiphyses did not develop. However, severe scar tissue around the epiphysis and the joint, apparently resulted in restricted growth of the epiphysis.

Growing children who sustain severe burns about the lower part of the leg and ankle joint should be observed carefully as one must anticipate possible latent growth retardation in the traumatized limb.— E. Nicholas Sargent, M.D.

SEFTEL, H. C., Malkin, C., Schmaman, A., Abrahams, C., Lynch, S. R., Charlton,

R. W., and BOTHWELL, T. H. Osteoporosis, scurvy, and siderosis in Johannesburg Bantu. *Brit. M. J.*, March 12, 1966, 1, 642–646. (From: Baragwanath Hospital and University of Witwatersrand, Johannesburg, South Africa.)

The authors report 32 Bantu patients with osteoporosis in association with scurvy and siderosis. All of these patients were severely osteoporotic, with obvious roentgenologic evidence of vertebral collapse, and the majority were disabled enough to require admission to the hospital. There were 26 males and 6 females with ages ranging between 30 and 60 years and a mean age of 47.

Backache was the principal complaint in all patients and in the majority it was the only symptom. Shortening of the vertebral column was reflected by a loss of height and a lumbar or dorsal gibbus was sometimes present. In 75 per cent firm enlargement of the liver was present and in 33 per cent the spleen was palpable.

Slightly less than half showed obvious evidence of scurvy. This was manifested clinically by hemorrhagic swelling of gums or bleeding into the subcutaneous tissues and muscles of the calf or posterior thigh. Some of the patients had subungual hemorrhages and hemarthroses and I patient had a hemorrhagic pleural effusion.

The diet of these individuals was high in carbohydrate, low in animal protein and fat and low in fresh fruit and vegetables, being similar to that of the general African population. One important exception, however, was that they all had a history of drinking larger than average quantities of the traditional Bantu beer and its numerous variants for many years. This beer is prepared from a variety of carbohydrate bases, the commonest being sorghum; the bases are acid in reaction and readily corrode the crude iron containers in which they are usually prepared. There is good evidence that they are the principal reason for the varying degrees of iron overload which are so commonly found in Johannesburg Bantu.

As regards the roentgenologic findings, there was an obvious decrease in density of the dorsal and lumbar spine associated with collapse of vertebral bodies. The collapse took the form of wedging, biconcavity ("codfish deformity") or marked flattening of the bodies (vertebra plana). The lumbar vertebral column was most severely affected with the number of vertebral bodies involved being 2 to 6. The lower dorsal and upper dorsal spine were less severely affected. In addition to the bony changes there was marked uniform increase in density of the hepatic and splenic shadows and almost invariably the density of the splenic shadow was equal to or greater than that of the liver. Enlargement of these organs was often seen. It is stated that such findings are usually due to heavy deposits of iron in these organs.

Biochemically, the serum calcium levels were found to be low, averaging approximately 4.5 mEq per liter. The serum phosphorus estimations were within normal range (2.5 to 4.5 mg./100 ml.). The serum alkaline phosphatase levels were within normal range (4 to 13 King-Armstrong units) except in 3 patients. Protein electrophoresis showed no abnormal protein fractions. However, serum albumin levels averaged 3.0 gm./100 ml. and serum globulin levels averaged 4.29 gm./100 ml. The hemoglobin levels were normal except in those patients who exhibited clinical evidence of scurvy. The levels of serum iron, total iron binding capacity and percentage saturation were estimated in all patients and averaged respectively, 152 µg./100 ml., 228 µg./100 ml. and 67 per cent for the osteoporotic patients. The serum iron and percentage saturation figures were above those in the controls and the total iron binding capacity was below that found in the controls.

Pathologically, osteoporosis was confirmed in 10 patients by biopsies of the iliac crest. The degree of siderosis was assessed in 18 patients by histologic examination of liver biopsy specimens and 17 of these were found to be severely siderotic and 1 moderately so. Two male patients went to necropsy. The cause of death probably was hepatic failure in one and in the other volvulus of the sigmoid colon. Both of these patients showed severe osteoporosis and severe siderosis.

Those patients who showed acute scurvy responded promptly to ascorbic acid. Interestingly, the roentgenologic signs of osteoporosis remained unchanged on treatment with ascorbic acid and calcium lactate, either singly or in combination. It is explained, however, that roentgenologic improvement would not be anticipated until after a 6 month period and at the time of the report enough time had not elapsed.

The authors give support to the theory of association of osteoporosis, scurvy and siderosis with evidence from the literature and postulate that all three of these findings may result directly from excessive consumption of the local alcoholic brews. However, other alternative explanations are given.—Lionel W. Young, M.D.

DORFMAN, HOWARD D., NORMAN, ALEX, and WOLFF, HANS. Fibrosarcoma complicating bone infarction in a caisson worker: a case report. J. Bone & Joint Surg., April, 1966, 48-A, 528-532. (From: Hospital for Joint Diseases, New York, N. Y. 10035)

A case of anaplastic fibrosarcoma arising at the site of an old infarct in the femoral shaft of a caisson worker is reported.

References to similar cases of sarcoma, developing at the site of a pre-existing non-neoplastic bone lesion such as Paget's disease, irradiation of either

diseased or normal bone, fibrous dysplasia, and chronic draining osteomyelitis are cited.

Fibrosarcoma complicating idiopathic bone infarction is also mentioned, but this is the only report in the literature of a sarcoma arising in a bone at the site of pre-existing caisson disease. In view of the large number of bone infarcts in caisson disease, sickle cell anemia, and other hematologic disorders, and of the rare occurrence of a complicating sarcoma, it would appear unlikely that a causal relationship is statistically justified.

In the event that bone pain is present in a caisson worker, and this symptom is supported roentgenographically by evidence of a destructive bone lesion replacing the calcified area of infarction, a malignant complication in the area of pre-existing bone disease should be considered.—E. Nicholas Sargent, M.D.

REINHOLD, H. Beitrag zur Adoleszentenkyphose (Morbus Scheuermann). (Contribution to the adolescent kyphosis [Morbus Scheuermann].) Radiol. Austriaca, 1966, 15, 249-258. (From: Strahleninstitut und Strahlentherapeutische Klinik der Medizinischen Akademie, Lüneburger Strasse 4, Magdeburg, Germany.)

Adolescent kyphosis is characterized by a wedging deformity of vertebral bodies, especially at the apex of the kyphotic curve. Its most frequent localization is in the lower thoracic and upper lumbar area. There is an irregular wavy contour of the upper and lower plates of the vertebral bodies, disk thinning and occasionally presence of an intraosseous Schmorl's node.

Symptoms and signs are insignificant in the majority of cases, but are more pronounced when an associated scoliosis develops. The condition can be clinically suspected when a kyphosis and scoliosis are present and when a spinal rigidity exists. The abnormal curves are irreversible. Pathologic changes are present in the cartilaginous plates, the vertebral bodies and the disks and are considered juvenile osteochondrosis. A fibrous transformation of the disks causes rigidity of the affected vertebrae and a fixation of the kyphosis.

Pathogenetic factors are similar to those of the juvenile osteochondritis of Perthes, Koehler, Schlatter and others. There is a disturbance of the ossification and a diminished growth factor. In the majority of cases, the disease is detected at ages 12 to 20 years. Men are more frequently affected than women. In the differential diagnosis, one has to exclude tuberculous spondylitis, traumatic changes, and rare systemic conditions.

The author statistically evaluated 12,000 cases with vertebral roentgenograms. Adolescent kyphosis was present in 3,284 (27 per cent) with a male preponderance of 3 to 2. Associated aseptic necrosis or juvenile osteochondritis of the types Perthes, Schlat-

ter and Koehler was encountered in 86 patients. There was a continuous increase of frequency from 1891 until 1920. For the past 40 years, however, the frequency has remained constant. Associated degeneration of the lumbosacral disk was frequently observed.

An early recognition of adolescent kyphosis is essential to effect orthopedic measures for the prevention of disabling deformities.—Ernest Kraft, M.D.

Moes, C. A. F., and Munn, J. D. The value of knee arthrography in children. J. Canad. A. Radiologists, Dec., 1965, 16, 226-233. (From: The Hospital for Sick Children, Toronto, Ontario, Canada.)

The authors investigated 114 cases for internal derangement of the knee. Ninety-eight of these were subjected to surgery. Arthrography was performed on 54 cases.

The most frequently encountered lesion in this series proved to be a diskoid meniscus which is a congenital anomaly in which the meniscus forms a solid plate that extends completely between the articular surfaces instead of forming a crescent shape. This lesion was found only on the lateral side.

The next most common lesion encountered was a torn meniscus which was found usually on the medial side, predominantly in males.

Other less common lesions described were mobile meniscus, cystic meniscus and hypertrophy of the infrapatellar fat pad.

Arthrography was correct in 90 per cent of those with a diskoid meniscus and in 88.8 per cent of those with a tear. Thus, the authors believe it to be a useful procedure.—Francis P. Shea, M.D.

BLOOD AND LYMPH SYSTEM

Collard, M. Une forme familiale de lipocalcigranulomatose avec calcinose artérielle. (A familial form of lipocalcigranulomatosis with arterial calcinosis.) J. de radiol., d'électrol. et de méd. nucléaire, Jan.—Feb., 1966, 47, 31–40. (From: Service de Radiodiagnostic de l'Université de Liège, Belgium.)

The term "lipocalcigranulomatosis" is to be preferred to "localized calcinosis" as being more precise and descriptive of the pathology. The disease appears after puberty, has a chronic evolution, is rarely associated with scleroderma, affects hands, feet, elbows and knees and gives articular pain of a rheumatoid character. The calcareous nodules are less than 2 cm. in diameter. (By contrast, interstitial calcinosis occurs under the age of 20 with rapid evolution, attacks the large joints and flexor muscles, is frequently associated with scleroderma, and produces mechanical difficulty by compression and limitation of motion. The nodules are more bulky.)

A few cases of a familial form have been reported in the literature, to which the author adds his 2 patients who were sisters in their fifties, and were found to have numerous smooth, dense, calcific nodules above their hands, elbows and feet. The arteries of the lower extremities, beginning sharply at the origins of the common femorals, were studded with fine punctiform or micronodular calcifications which did not resemble the ordinary plaques of atheromatosis, nor was there evidence of the latter lesion in the aorta or iliac arteries.

The author states that the arterial lesions suggest that a vascular dystrophy may precede the calcareous deposits.—Frank A. Riebel, M.D.

GENERAL

Belli, M., and Perotti, B. A. battery-operated photofluorography installation mounted in a vehicle-initial trial. *Panminerva med.*, Dec., 1965, 7, 487-489. (Address: Prof. M. Belli, Consorzio Provinciale Antitubercolare, Milano, Italy.)

With the development by Generay of a battery operated source of energy called the Independent, the use of vehicles for photofluorography became a reality.

Two standard 12 v. batteries are required for the unit. The unit is provided with a battery charger which can utilize any available low power alternating current.

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If the batteries were fully charged (26 v.) it was possible to take up to 3,000 fluorograms without additional supply of electricity. However, the output after 2,000 diminishes considerably, thus requiring an increasing exposure time.

It has been found that the use of the Independent in the radiographic field means a reduction in dosage varying between 30 to 50 per cent relative to single phase X-ray units. There is also a reduction of dosage when compared to the three-phase X-ray generators.—Forrest Arnoldi, M.D.

Hems, G. Detection of effects of ionizing radiation by population studies. *Brit. M. J.*, Feb. 21, 1966, 1, 393–396. (From: Radiological Protection Service [Ministry of Health and Medical Research Council], Sutton, Surrey, England.)

Up to the present time the harmful effects of low doses of radiation given at low dose rates (less than I rad per year) have not been demonstrated, but the possible hazards have been estimated. These estima-

tions are based on extrapolated data obtained from the measured effects of high doses delivered at high dose rates. A population study is necessary to determine directly effects such as the increased incidence of leukemia or genetic mutations in these large groups of people, e.g., those exposed to increased fallout.

Such a study poses many problems, not the least of which is determining the minimum population size required to produce statistically significant data. In the detection of genetic effects, for example, the size would be governed by the mutation rate of the dominant characteristics selected, the doubling dose of radiation required, the number of mutations studied and the confidence limits desired.

Three different estimates have been given for the size of the population necessary to detect an increased incidence of leukemia. These estimates are based on an exposure of 1 rad/year and will vary according to the amount of background radiation received. In addition, the altitude of the area in question will affect significantly the amount of cosmic radiation received by the population studied.

In those occupationally exposed radiation workers who are permitted whole-body doses of 5 rads/year, it is calculated that the minimum population size required to prove a significant rise in the annual number of cases of leukemia would be 1.55 × 105 man years—if each worker received the maximum 5 rads. In the United Kingdom in 1960, there were approximately 2,249 workers exposed to a dose in excess of 1.5 rads—less than 2 per cent of the required minimum even if it is assumed that they all received the maximum 5 rads.

The author concludes, therefore, that populations studied to date are smaller than the theoretical minimum required and that future studies will pose many practical problems which will make significant data difficult to obtain.—Howard West, M.D.

BOYD, J. T., BROWN, W. M. COURT, VENNART, J., and WOODCOCK, GILLIAN E. Chromosome

studies on women formerly employed as luminous-dial painters. *Brit. M. J.*, Feb. 12, 1966, 1, 377–382. (Address: J. T. Boyd, M.B., M.R.C. Statistical Research Unit, University College Hospital Medical School, London, England.)

In the United Kingdom luminizing has been carried on since 1914. At the onset of World War II this industry was considerably expanded and, in view of the well known problems which had occurred in the U.S., was placed under control of the Ministry of Labor. Since then, no serious damage attributable to ingestion of radium has been reported. Long term studies on this group of workers are continuing, however.

The present report is concerned with a study of chromosome damage in cells taken from blood cultures of 62 women luminizers. The authors' combined experience extends from the early days of the industry through the middle fifties, with the majority of their experience concentrated in the war years of 1939 to 1945.

The subjects were divided into 3 groups according to the estimated body radium content as follows: non-measurable to 0.04 μ c; 0.05-0.09 μ c; and 0.10 to 0.66 μ c

0.56 µc

Following study of the cultures from each subject the cells were assigned to one of 3 categories: (A) cells with no obvious structural abnormality; (B) cells showing a chromatid gap, chromatid break, or chromatid interchange; and (C) cells with any type of structural abnormality. This latter group was further subdivided into "unstable" and "stable" abnormalities depending upon the type of chromosome alteration present.

The proportion of abnormal cells in the luminizer group (4.5 per cent) was higher than in the control group (2.8 per cent). In addition, the data displayed a consistent trend of increasing structural abnormality with increase in activity of radium in the body.—

Howard West, M.D.



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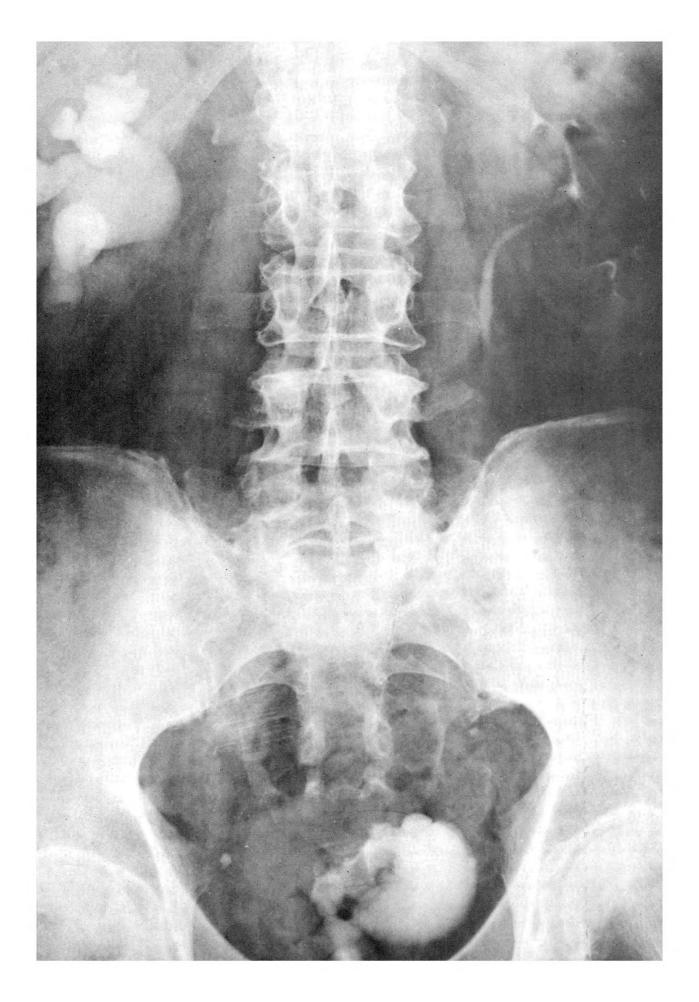
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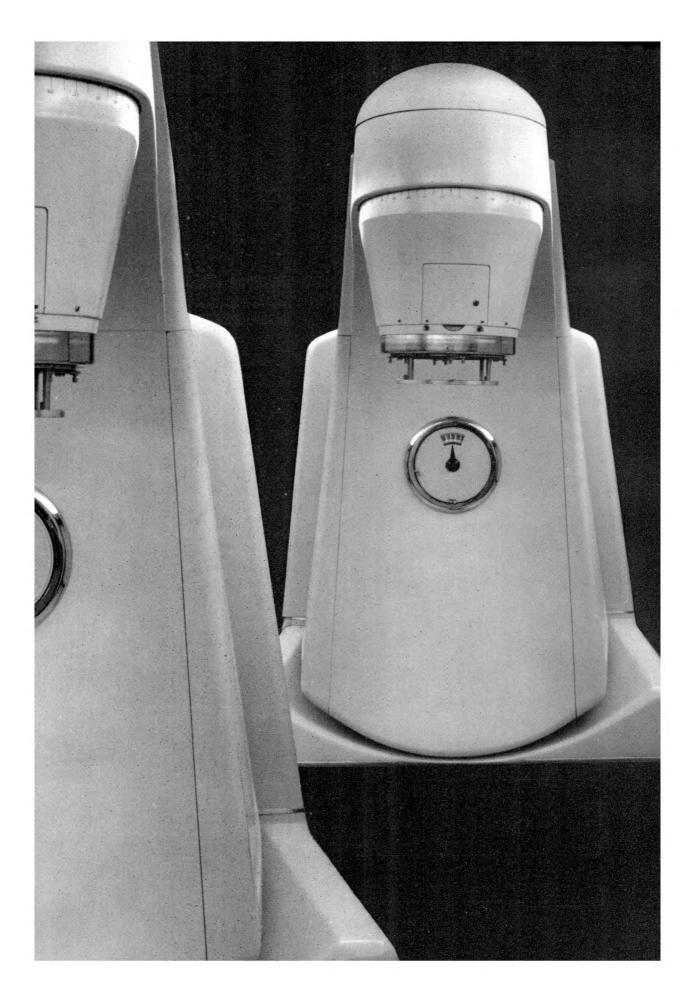
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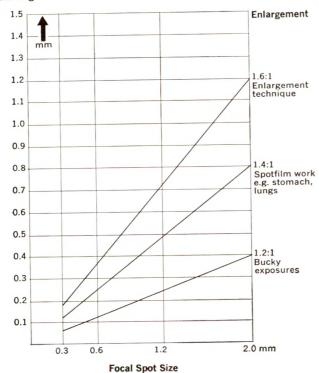
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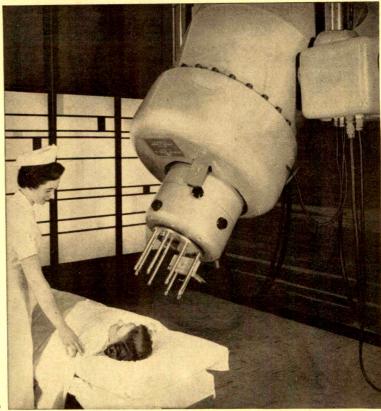
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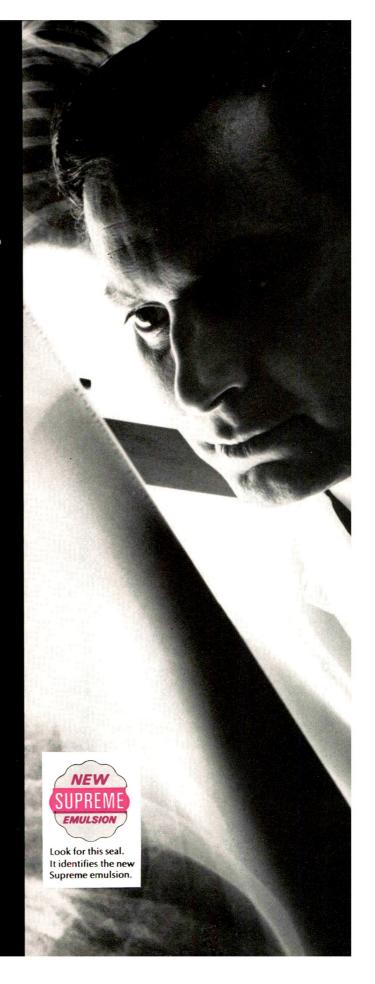
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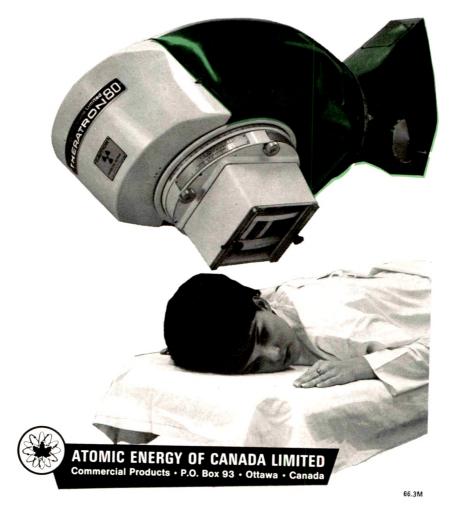
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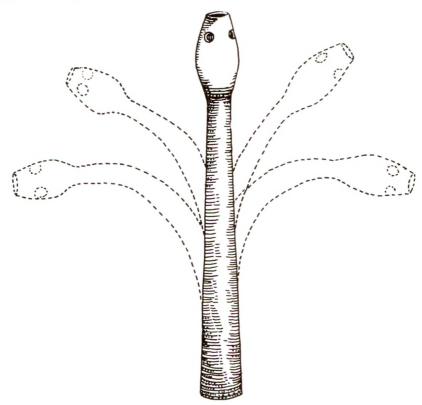
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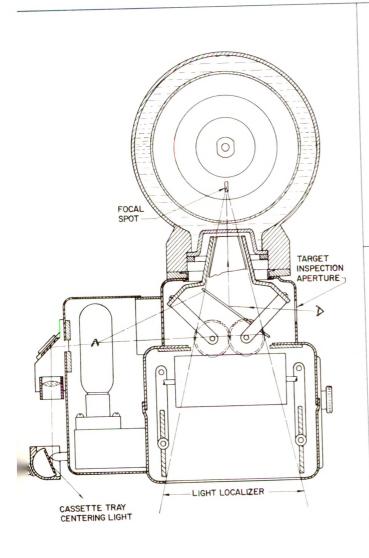
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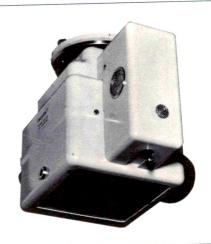




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ROBERT P. BARDEN Hickey Lecturer, 1966

THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

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No. 2

GLIMPSES THROUGH THE PULMONARY WINDOW*

INTERPRETATION OF THE RADIOLOGIC EVIDENCE IN DISORDERS OF THE LUNGS

HICKEY LECTURE, 1966

By ROBERT P. BARDEN†

Preston M. Hickey is remembered by this Annual Oration because of unique qualities, which have become blurred with time. Let me sharpen again the picture of this pioneer in radiology. He left a busy private practice in Detroit in his middle years to become Professor of Radiology at the University of Michigan in 1922. Here, in a remarkably short time, he developed a center for the academic practice of the newly born specialty of radiology and endowed it with his own international reputation. At the time of his death in 1930 at the age of 65 years, he was a great and famous man. Most of us never knew him; therefore, I wish to quote briefly from the words of those who did.

In 1937, the first Hickey Memorial Lecturer, Dr. A. W. Crane of Kalamazoo, another famous pioneer in radiology, said, "We who knew him, know that Preston M. Hickey is forever identified with the development of roentgenology. He took up the roentgen ray when it was a scientific curiosity and laid it

down as one of the foundations of modern medicine."

In 1939, the third Memorial Lecturer, Dr. B. R. Kirklin of Rochester, Minnesota, also a great and famous man, said of Dr. Hickey, "All that he gave to roentgenologic science will be mingled in the common heritage of future roentgenologists who will scarcely recall the name of the giver. But the impress of his fine character on the men whom he trained, the kindliness that he showered on all whom he knew, and the gratitude of his patients for his sympathetic professional care, will be passed on as a leaven without end. No man could have a more enduring monument than this."

In 1904, Dr. Hickey contributed a paper to the Transactions of the American Roentgen Ray Society titled "The Interpretation of Radiographs of the Chest."6 It is not the content of the paper but his concluding remarks which arrest one's attention. They are as true today as they were then; and I quote, "The marked improvement in radiographic

† From the Department of Radiology, Chestnut Hill Hospital, Philadelphia, Pennsylvania.

^{*} Presented at the Meeting of the Wayne County Medical Society, the Wayne State University College of Medicine and the Detroit Roentgen Ray and Radium Society, Detroit, Michigan, March 3, 1966.

technic has resulted in adding a diagnostic measure of great value to our armamentarium of already tried methods. This means of thoracic exploration, while already developed enough so as to be of considerable diagnostic value, is destined through future study and experiment to yield conclusions which will be still more valuable."

Therefore, I am persuaded that he might have been interested, some 62 years later, in the direction taken by the art he began; and would listen with a sympathetic and understanding ear to my remarks tonight on a similar topic, to wit: "Interpretation of the Radiologic Evidence in Disorders of the Lungs."

TO INTRODUCE this subject, it is necessary to propose a concept which can be expanded later in discussing various abnormalities in pulmonary function. During phylogenetic development, the lungs of mammals have been folded inside the body and connected to the external atmosphere only by a system of slender tubes through which air flows in both directions. When one compares this arrangement with the gills of fishes, for example, where O2 in the external environment is brought in direct contact with the respiratory capillaries, one appreciates how much more vulnerable is the lung of man to many different insults which lead to obstruction in the tracheobronchial system.

However, strangely enough, man may soon be able to return to the sea using artificial gills which extract O₂ from water and present a primary barrier between the inefficient human lung and its aqueous environment. Dr. Walter L. Robb, of the General Electric Laboratories in Schenectady, has developed a new thin film of silicone rubber which can draw oxygen out of water while the water itself is held back. Experimental animals in a cage enclosed by this synthetic "breathing" film have lived for several days under water without additional oxygen.8

Let us now consider the radiologic evidence which accompanies some examples of

abnormal pulmonary function occurring in primary disorders of the lungs. To do this, one must project the static information from the film into the dynamic concepts it implies; much as the famous pathologist who once said that, when he looked at a microscopic section of a tumor, he tried to imagine what had occurred to bring these cells to their present state and what was their potential for the future.

In this exercise, it is convenient to subdivide the examples into 4 arbitrary groups: those showing disturbances in pulmonary capacity; those where diffusion or gas exchange across the alveolar membrane is impaired; those where ventilation is uneven; and those with altered pulmonary circulation.

CAPACITY

The primary function of the lungs is gas exchange (O₂ and CO₂) between the external atmosphere and the blood. This requires a sufficient volume of gas and area of surface interaction; and, in the special case of mammals and man, easy movement of gas in and out of a complicated system of airways.

Congenital cystic disease of the lungs or congenital bronchiectasis is an example of deficient pulmonary capacity in which the number of respiratory units is reduced greatly (Fig. 1). In this condition, clusters of large air spaces surround large bronchi, and the normal fine division and subdivision of airways and air sacs have not occurred. In the normal lung the surface area available for gas exchange in the alveoli has been estimated at 100 sq. m.¹⁰ It is obvious that the patient with congenital cystic disease has greatly reduced capacity for O₂ and CO₂ exchange because of the reduced area of interaction.

Another example of a common condition with progressive loss of effective pulmonary capacity is seen in the patient with chronic bronchitis and emphysema (Fig. 2, A and B). In this situation, the thorax becomes fixed in the inspiratory attitude and there is increasing difficulty in moving air in and

out. The bellows action of the ribs and diaphragm is lost and the elastic recoil of the lungs disappears. The patient develops the clinical state of chronic pulmonary insufficiency with imminent pulmonary or cardiac failure.

A third example of altered pulmonary capacity is seen with pulmonary fibrosis, such as Boeck's sarcoid produces. The lungs of these patients are often stiff and the supporting structures are enlarged considerably at the expense of the air spaces. This results in great difficulty in moving air in and out through the bronchial tree, and there are considerably fewer functioning alveoli than normal to handle it. In some ways, the disability which occurs in fibrosis resembles that in congenital cystic disease but for entirely different reasons. Fibrosing conditions encroach on functioning respiratory units while in cystic disease the units are deficient at birth.

Diseases which produce impairment of movement of air often do so through their effect on the bronchial tree, which is vulnerable because of its design. The same set of tubes is used for traffic going in and traffic going out, and thus is in double jeopardy. Furthermore, even under normal circumstances, the bronchi are reduced in caliber during expiration, although the same volume of gas must move out, as moved in.

DIFFUSION

There are some pulmonary disorders where gas exchange across the alveolar membrane is impaired, even when the mechanics of breathing are normal, ventilation throughout the lungs is even, and pulmonary blood flow is adequate. This is encountered when the interstitial tissues are involved in inflammatory processes or by edema. One might consider, then, as a classic example of impaired diffusion capacity, the effects of submersion in sea water.2 In this situation the excess osmotic pressure of the inhaled salt water pulls fluid from capillaries in alveolar walls into the interstitial spaces 9 (Fig. 3, \mathcal{A} and \mathcal{B}). This fluid is interposed between air in the alveoli and



Fig. 1. Bronchogram of a young man with so-called "congenital cystic disease" of the lungs. The opaque material has filled large short bronchi, surrounded by clusters of large air sacs. Since the normal fine division and subdivision of bronchi and air sacs have not occurred, the surface area available for gas exchange in the alveoli is greatly reduced. This impairs seriously the capacity of the lung to function in O₂ and CO₂ exchange.

blood in the capillaries and prevents diffusion of O₂ and CO₂. A similar barrier, of course, may occur when fluid or exudate collects in alveoli themselves.

Again, many systemic diseases have as target organs, arterioles and capillaries, particularly the connective tissue disorders in which vasculitis is prominent. In many of these conditions, one may peer through the pulmonary window and behold the results of damage to the small vessels of the body as reflected in the lung. Increased permeability of arterioles and capillaries pro-

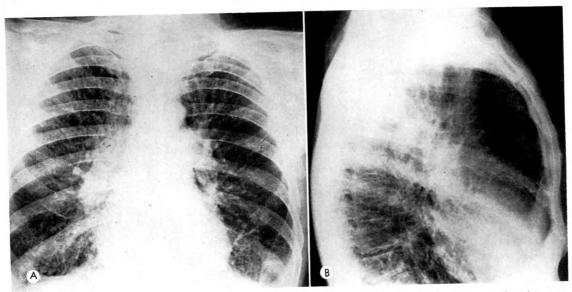


Fig. 2. (A and B) Roentgenograms of a 60 year old white man with chronic cough and increasing dyspnea. Note that the thorax appears fixed in the inspiratory attitude, which implies that the mechanics of breath ing are greatly impaired. The lungs are overdistended, but very little air flows in and out with respiration. Note, also, the enlargement of the main pulmonary arteries which probably indicates pulmonary hypertension due to obliteration of many of the peripheral arterioles and capillaries.

duces a pulmonary edema of peculiar distribution, in the shape of a "butterfly" or "batwing" (Fig. 4). One explanation for the characteristic pattern of this edema associated with increased capillary permeability is the anatomic division of the

lung into a medulla and cortex, as determined by the differences in the vessels in the center and periphery¹ (Fig. 5).

Or, as an example of a chronic condition with a diffusion barrier, one may cite the patient who is a pulmonary invalid, suffer-

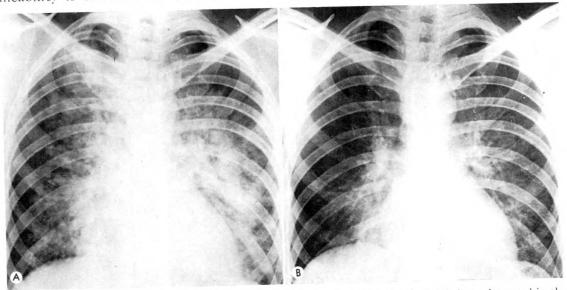


Fig. 3. (A and B) Roentgenograms of a young naval aviator who was rescued after being submerged in the ocean. The initial pulmonary edema (A) cleared in 24 hours (B). The edema is due to the excess osmotic pressure of sea water, which pulls fluid from capillaries in the alveolar walls into the interstitial spaces. This layer of fluid presents a barrier to diffusion of O_2 and CO_2 across the alveolar-capillary membrane.

ing from asbestosis. The inhaled asbestos fibers produce a chronic interstitial pneumonia and marked inflammatory thickening of alveolar walls. Unlike edema, this diffusion deficit is progressive and irreversible.

UNEVEN VENTILATION

One may turn now to the most common disorder of pulmonary function, namely, uneven distribution of inspired air throughout the lungs (Fig. 6, A and B). Patients with this condition may suffer from chronic anoxemia because large portions of their lungs contain air which does not circulate with respiration and thus cannot be renewed. Uneven ventilation is present in varying degrees in all aging lungs, and may lead to vascular shunts of minor or major proportions when pulmonary artery blood circulates through dead air spaces to reach the pulmonary veins. Irregular ventilation may exist when the patient has normal mechanics of breathing, normal lung capacity, and normal pulmonary circulation.

The radiologic evidence of diffuse irregu-

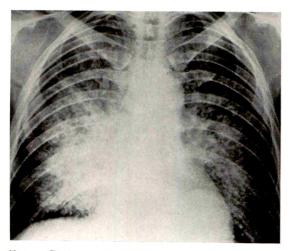


Fig. 4. Roentgenogram of a 50 year old white man who was suffering from periarteritis nodosa and developed sudden dyspnea. The edema fluid presents a characteristic "butterfly" pattern which occurs also in other diseases with increased permeability of pulmonary capillaries. This pattern corresponds to the "medullary" portion of the lungs where "respiratory" capillaries are most numerous; therefore, the diffusion barrier produced by this edema is all the more significant.

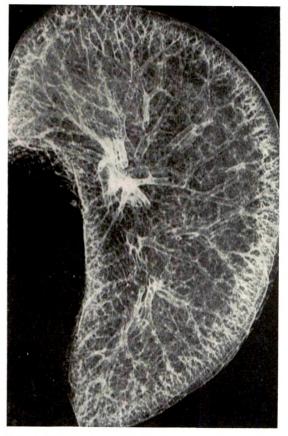


Fig. 5. Roentgenogram of a thin slice of lung after injection of the pulmonary arteries. Note the abrupt change in the number of visible small vessels, between "medulla" and "cortex." Actually, there are many more "respiratory" capillaries in the medulla, but these are too small to be seen. (Courtesy of Dr. Charles B. Oderr, New Orleans, La.)

lar ventilation consists of alteration in the normal pattern of the vascular markings, often seen best in lateral or oblique views. Since the blood vessels parallel the airways, the regular symmetric pattern of normal markings indicates equal dispersion of air around them. When the pressure of the inspired air is uneven, the vascular markings become distorted and reflect the loss of the delicate balance present in the normal.³

Although the cause of the lung distortion which accompanies uneven ventilation is often obscure, one can, occasionally, trace its relentless progress in certain diseases where interstitial fibrosis is prominent, as

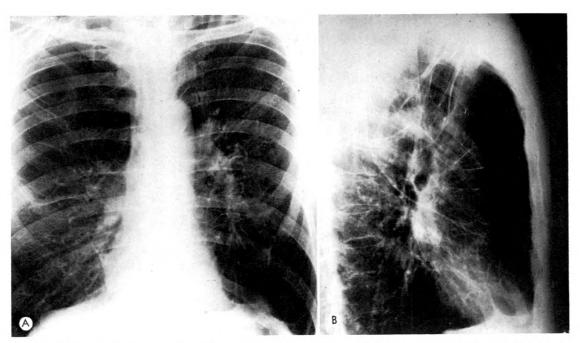


Fig. 6. (A and B) Roentgenograms of a 45 year old white man with dyspnea, cough and marked decrease in exercise tolerance (chronic pulmonary insufficiency). Note the bullae in the right upper and left lower lobes which contain large amounts of "dead" air. Since the blood in the pulmonary arteries which flows through these areas does not receive O₂, a vascular shunt is present. Note, also, the irregular pattern of the lung markings in the lateral view. This indicates nonuniform distribution of air throughout the lungs.

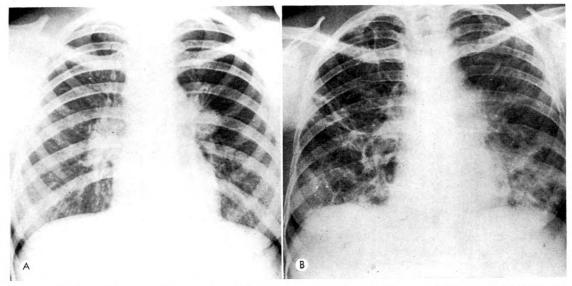


Fig. 7. (A) Roentgenogram of a 25 year old Negro woman with Boeck's sarcoid. The mediastinal lymph nodes are enlarged. The lungs appear well ventilated. (B) Roentgenogram of the same patient 4 years later. Note that extensive fibrosis of the interstitial tissues of the lungs has resulted in very irregular ventilation. In addition, one can anticipate a decreased volume of air in the lungs and difficulty in moving air in and out because of the increased fibrous tissue, which is not elastic. The patient died later of pulmonary failure.

in patients with Boeck's sarcoid (Fig. 7, A and B).

With these examples in mind, one may wonder at the mechanisms which maintain a constant pulmonary ventilation to blood flow ratio in all parts of the lung, in health. This precise matching ensures maximum efficiency of gas exchange, and it is the dislocation of this ratio of air to blood which leads to pulmonary insufficiency and failure in many acute and chronic disorders of the lungs⁴ (Fig. 8, \mathcal{A} and \mathcal{B}).

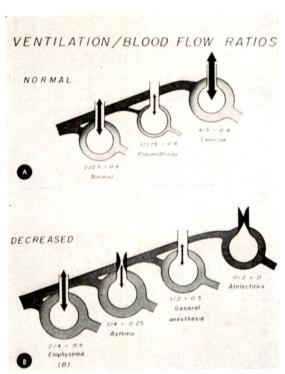


Fig. 8. (A) Diagram showing the normal relationship between alveolar ventilation and capillary blood flow under different conditions. Note that in the resting normal individual, each lung receives 2 liters of air and 2.5 liters of blood giving a ratio of 0.8. Maximum efficiency of respiration is accomplished if this ratio is maintained throughout the lung even though the total volumes involved may be larger or smaller. (B) Diagram showing disturbance of the alveolar-blood flow ratio in conditions producing decreased ventilation without decreased blood flow. This causes vascular shunts which may return large amounts of unoxygenated blood to the systemic circulation. (Courtesy of Dr. Julius Comroe and collaborators and the Year Book Medical Publishers, Chicago, Ill.)



Fig. 9. Roentgenogram showing opacification of right bronchial artery after catheterization. Chronic disease in the right lower lobe has caused enlargement of the bronchial artery, which now communicates directly with a large pulmonary vein seen coursing upwards and medially toward the hilus. (Courtesy of Dr. Manuel Viamonte, Jr., Miami, Fla.)

CIRCULATION

If the tracheobronchial tree is vulnerable by virtue of its design, the vascular apparatus of the lungs, on the other hand, is remarkably efficient. The pulmonary vessels form a vast sponge, which soaks up blood as necessary. This ebb and flow of blood is possible because of the extremely low pressures in the pulmonary vessels, which favor easy shifts in direction of flow with slight local pressure changes. To this facility is added the ease of shunting blood between large vessels because of the many potential communications between pulmonary arteries and veins and between pulmonary and bronchial arteries (Fig. 9).

In conditions such as atelectasis or where

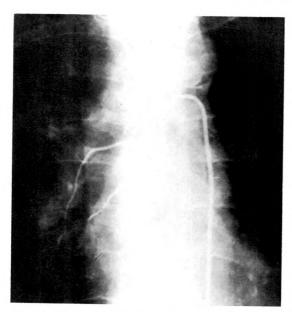


Fig. 10. Normal right bronchial artery, opacified through a catheter passed up the aorta. Note the slender caliber and meandering course of this vessel. It seems to have no large branches and provides relatively little blood. (Courtesy of Dr. Roy Greening, Philadelphia, Pa.)

peripheral pulmonary vessels are obliterated, this re-direction of pulmonary blood to functioning lung tissue provides a vital adaptation. And when gradually increasing obstruction to flow in *pulmonary* arteries occurs, as it does in some chronic inflammatory states, the *bronchial* arteries hypertrophy and take over the load of CO₂ and O₂ transport¹¹ (Fig. 10 and 11).

Some patients with recent pronounced dyspnea may show radiologic evidence of a sudden major deficit in pulmonary artery blood flow when conventional roentgenograms are inspected closely. One may recognize a local or general reduction in number and size of the normal pulmonary arteries and veins, both in the hilar regions and in the periphery. Pulmonary arteriograms may demonstrate a solitary or major obstruction in an artery and lead to surgical removal of an embolus, which may save the patient's life (Fig. 12, \mathcal{A} and \mathcal{B}).

Furthermore, multiple small pulmonary emboli are common, are frequently overlooked, have a lethal potential, and often occur with atypical symptoms and signs. The use of radioiodinated macro-albumin as a tracer, injected intravenously, provides a safe, simple and accurate method of detecting pulmonary emboli quickly (Fig. 13, \mathcal{A} and \mathcal{B}).

Less common and more insidious and difficult of diagnosis are the chronic obliterative diseases of pulmonary vessels such as arteriolar sclerosis. These lead to a deficit of circulating blood in relation to available alveolar air, and chronic anoxemia results. Pulmonary hypertension and right ventricular failure may ensue (Fig. 14).

SUMMARY

We have presently considered in brief review some conditions in which profound changes in the lungs may be recorded by radiologic methods; and by this means the

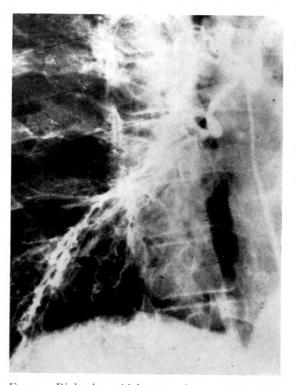


Fig. 11. Right bronchial artery in a patient with chronic inflammatory disease in the right lower lobe. Note the large caliber, tortuous course, and several branches of this vessel, which has hypertrophied in reponse to the infection. (Courtesy of Dr. Manuel Viamonte, Jr., Miami, Fla.)

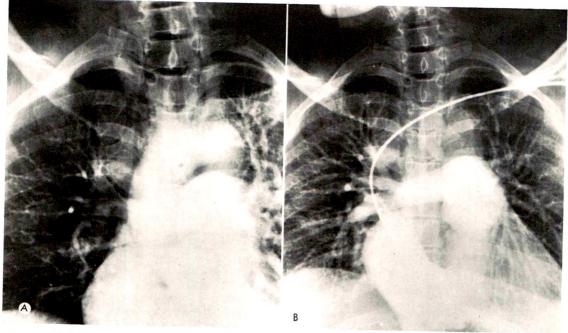


Fig. 12. (A) Intravenous pulmonary arteriogram showing complete obstruction of the right main pulmonary artery by a large embolus. The sudden occlusion has caused overloading of the pulmonary arteries in the left lung. The patient was in shock. (B) Repeat pulmonary arteriogram, in the same patient, after successful surgical removal of the embolus. Note caliber of pulmonary vessels and compare with A. (Courtesy of Dr. Roy Greening, Philadelphia, Pa.)

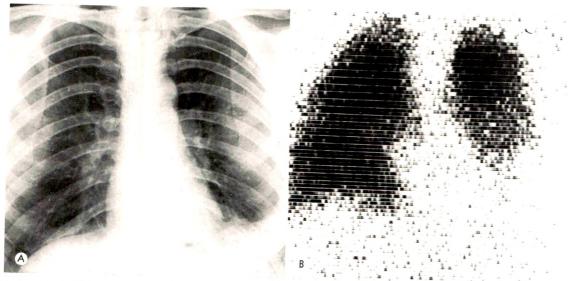


Fig. 13. (A) Roentgenogram of a 30 year old white woman with cough and pain in the left lower chest. Note the local consolidation at the left base which probably involves the pleura, and may be an infarct. (B) Scan of the lungs, I month later after intravenous injection of radioactive human macro-albumin. The albumin mass lodges in capillaries in which blood is circulating, and hence identifies areas of normal perfusion. Note absence of radioactivity in left lower lobe, corresponding to the infarct seen on the roentgenogram. Note also a deficit in the right lower lobe, which represents another infarct, not demonstrated on the roentgenogram.

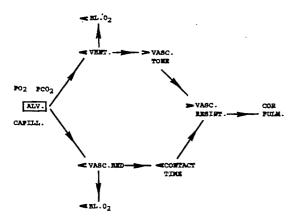


Fig. 14. Diagram showing that hypoventilation of alveoli or decrease in the pulmonary capillary bed may produce the same end result; namely, anoxemia, pulmonary hypertension, and eventual failure of the right side of the heart. Roentgen evidence of deficits in ventilation or blood flow in the lungs should impress the radiologist with the inevitable physiologic consequences.

initiated may be afforded the satisfaction of glimpses through the pulmonary window. It is all too evident, however, that now we see many things through a glass rather darkly; but we may hope that, with greater knowledge and the inevitable expansion of our specialty, the day will come when radiologic examination of the chest will provide us with more sophisticated information than we recognize at present.

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I wish to thank, Drs. Charles Oderr, Roy Greening, Manual Viamonte, Jr., and Julius

Comroe and his collaborators for their generous contributions of some of the material used in this Lecture.

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THE LATERAL ROENTGENOGRAM IN PULMONARY EDEMA*

By D. C. GLEASON, M.D., \dagger and R. E. STEINER, M.D. LONDON, ENGLAND

PULMONARY edema appears roentgenologically in a variety of ways: as interstitial pulmonary edema, usually associated with left sided heart failure or mitral valve disease, or, as acute intra-alveolar pulmonary edema. This, too, is often associated with acute left sided heart failure or renal failure, in which case it is sometimes referred to as "uremic edema."

In this paper we shall re-assess some observations made of the roentgenologic findings in acute pulmonary edema by a study of patients with heart failure and renal failure. We want to reconsider particularly the appearances of intra-alveolar pulmonary edema and the reasons for its distribution.

It has been said that roentgenologically intra-alveolar pulmonary edema presents in a distinct way, with a central distribution of the edema fluid, as first described by Day et al.⁵ and later restated by Coe and Otell,⁴ and Werkenthin.²⁷ Nessa and Rigler²¹ described the lesions more accurately and coined the term "butterfly" shadows. Most workers subsequently have stressed the central distribution of this edema. The pathologic and roentgenologic appearances were analyzed by Doniach⁷ and the roentgenologic appearances again by Jackson¹⁸ and Hodson,¹⁷ who coined the term "batswing" shadows.

Herrnheiser and Hinson¹⁶ suggested an anatomic and functional difference between the central core of the lung and the periphery as the main cause for the central distribution. Some further observations by Prichard *et al.*²³ tended to agree with this interpretation of an anatomic difference. These authors demonstrated a distinctive

flow pattern in acute animal experiments when injecting contrast material into the main pulmonary artery.

The roentgenologic evidence for the central distribution of pulmonary edema is indefinite since most studies to date have relied mainly on frontal chest roentgenograms and not on lateral studies. Grainger, 12 discussing the distribution of acute intraalveolar pulmonary edema, remarked on the central distribution of the shadows and their symmetric appearances, but hinted at a possible gravity effect, suggesting that the edema could be basal, unilateral, or even apical. A similar suggestion was put forward by Steiner.26

Barden¹ discussed the correlation of the roentgenologic appearances of pulmonary edema with its various causes, but added little to the explanation of the unusual distribution of acute pulmonary edema.

Another explanation for the production and distribution of pulmonary edema was offered by Borgström et al.,3 who experimentally altered the pulmonary capillary permeability. They injected the bronchial arteries in one group of dogs and the pulmonary arteries in another, using sodium desoxycholate to alter the permeability of injected vessels. In the first group (bronchial vessels), the edema produced was central and especially perihilar. It was seen in the peribronchial and perivascular spaces; it was interstitial. When the pulmonary arteries were injected, there was alveolar edema which was confined to the segments of the lung supplied by the artery.

There is still no definite evidence that pulmonary edema in patients with renal failure, the so-called "uremic" edema, is an

^{*} Presented at the Sixty-seventh Annual Meeting of The American Roentgen Ray Society, San Francisco, California, September 27–30, 1066.

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TABLE I

	The state of the s	
Patient	Diagnosis	Blood Urea (mg. %)
w.w.	Hypertension	98
A.M.	Myocardial infarction	183
N.T.	Pulmonary infarction	
	? Myocardial infarction	71
M.H-R	Myocardial infarction	56
A.P.	Aortic valve disease	98
H.B.	Mitral and aortic valve	64
S.T.	Congenital mitral incompetence, coarctation of the	•
73. 117	aorta	61
R.W.	Ischemic heart disease	Not
n.a		available
E.C.	Cardiomyopathy	25
N. St.J.	Constrictive pericarditis	36
B.M.	Myocardial infarction	54
F.J.	Aortic stenosis	122

entity in itself and independent of left sided heart failure, as suggested by a number of workers.^{2,11,15}

There are others^{8,17,22} who suggested that uremic edema is largely dependent on the presence of left sided heart failure, but modified by the uremia, probably affecting the permeability of the capillary membranes. Roentgenographically, the appearances are very similar and no distinction on the basis of underlying etiology is possible.

METHOD

Twenty patients were studied roentgenologically by means of anteroposterior and lateral chest roentgenograms taken on the ward. Twelve patients had heart disease and 8 renal failure (Table I and II). Ten of the 12 cardiac patients had elevated blood urea levels. Of the 8 patients with renal failure, 5 had evidence of congestive cardiac failure as judged by clinical examination, cardiographic findings and the roentgenologic assessment of the heart. In I case congestive cardiac failure was uncertain, but possible and I patient had definite evidence of hypervolemia. The patients, with one exception, were too ill to be examined in the X-ray Department and ward unit roentgenograms were obtained. In the majority of cases, these roentgenograms were repeated daily, or sometimes even twice daily, during the period of their acute illness. A record was kept of the patients' posture before the roentgenographic examination was carried out.

The roentgenograms of each patient were studied to determine the pattern and distribution of pulmonary edema and the way in which this changed during the illness. An attempt was made to distinguish between intra-alveolar and interstitial pulmonary edema.

INTERSTITIAL PULMONARY EDEMA

This was diagnosed by the following criteria: (1) Peripheral septal lines (Kerley's B lines); 19 (2) long septal lines extending from the hilar region to the periphery (Kerley's A lines); 19 (3) perihilar haze; and (4) peribronchial and perivascular "cuffing" which is due to an accumulation of edema fluid in the loose connective tissue spaces surrounding these structures 14 (Fig. 1, A, B and C). The fluid causes thickening and poor definition of the bronchial wall and blurs the edges of the end on vessels.

INTRA-ALVEOLAR PULMONARY EDEMA

This was diagnosed by the following criteria: confluent shadows of no specific distribution, more or less uniform in density with somewhat ill-defined margins. The appearances are similar to and often indistinguishable from other causes of pulmonary consolidation, such as pneumonia or infarction. On serial roentgenograms, these shadows frequently change their appearance and distribution.

It was often difficult in the lateral roentgenogram to localize the segmental distribution of the edema because of the overlap of the two lungs. It was impractical to take oblique roentgenograms with ill patients in bed.

TABLE II
RENAL CASES

Patient E.B.	Diagnosis	Blood Urea (mg. %)	Associated Factors			
	Acute nephritis	315	Doubtful C.C.F			
N.C.	Polyarteritis nodosa	490	C.C.F.			
E.T.	Chronic pyelonephritis	550	_			
J.E. T.N.	Chronic glomerulonephritis	I 44	Hypervolemia			
A.H.	Chronic pyelonephritis	340	C.C.F.			
A.G.	Chronic pyelonephritis	695	C.C.F.			
P.B.	Chronic pyelonephritis Chronic glomerulonephritis	300	C.C.F.			
1.0.	Malignant hypertension	370	C.C.F.			

C.C.F. = Congestive cardiac failure

Nevertheless, we were usually able in these cases to make an accurate localization in respect of the segmental anatomy.

RESULTS

An analysis of the distribution of pulmonary edema relying on the lateral roentgenograms shows a pattern very different from that suggested on the frontal roentgenogram alone (Tables III, IV and V). The Classic "Batswing" Shadows. Six of the patients were considered as fitting into the so-called "batswing" pattern when judged on the frontal roentgenogram alone (Table III). The lateral roentgenogram, however, showed that, in addition to the central distribution of the edema, lung segments anterior and posterior to the hilus were also involved. Three of these patients showed evidence of interstitial pul-

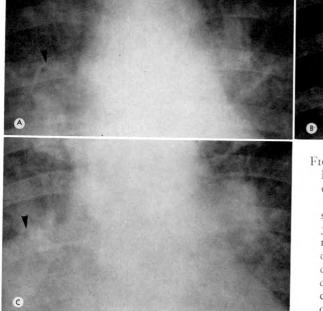




Fig. 1. Patient A.S., female, aged 59 years. Hypertensive for 10 years, several attacks of congestive heart failure, albuminuria.

(A, B and C) Localized anteroposterior studies of the hilar regions. (A, November 30, 1962; and C, July 13, 1963) Studies made during attack of left ventricular failure demonstrate the perihilar haze. There is poor definition of hilar blood vessels and bronchi due to perivascular and peribronchial cuffing. (B, April 23, 1963) Study made out of failure demonstrates the perihilar shadows much clearer. The end-on vessels and

bronchi are clearly defined. The arrow marks an upper lobe end-on artery and bronchus.

TABLE III
CLASSIC "BATSWING" EDEMA

Patient	Diagnosis	Classic Central	Intra-alveo Additional Lu	Interstitial Edema		
ratient	Diagnosis	Edema	Right Lung	Left Lung	Edema	
E.B.	Renal	+	Anterior segment upper lobe			
E.T.	Renal	+	Apical, posterior upper lobe	None		
M.H-R	Cardiac	+	Mid and low exception	Uncertain		
A.P.	Cardiac	+	Anterior segment upper lobe Posterior segment upper lobe Apical posterior upper lobe		Slight (cuffing; S.L.)	
R.W.	Cardiac	+	Middle lobe, lower lobe, basal	Marked (cuffing; P.H.H.; S.L.)		
В.М.	Cardiac	+	Probably ant uppe	Marked (cuffing P.H.H.; S.L.)		

P.H.H.= Perihilar haze
Cuffing= Peribronchial
Perivascular
S.L. = Septal lines

monary edema in the periphery of the lungs also (Table III; and Fig. 2, A and B; and 3, A and B).

Bilateral Edema but Not Classic "Bats-wing." In 5 patients, the edema was bilateral but not equal in the two lungs. In 1

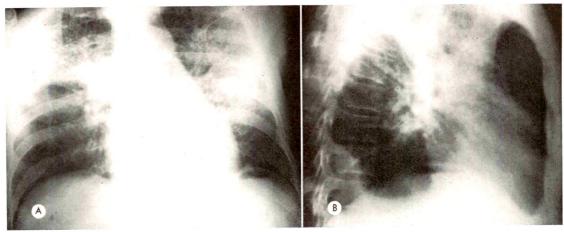


Fig. 2. Patient E.T., male, aged 51 years. Chronic renal failure due to pyelonephritis.

(A) Anteroposterior ward unit roentgenogram shows the classic "batswing" shadows due to edema in both mid zones with clear apices and bases. (B) Lateral roentgenogram shows the central distribution of the edema, but there is also evidence of some upper lobe edema; the lower lobe, anterior segment of upper lobe and middle lobe are clear. Small pleural effusion is present in the paravertebral gutter.

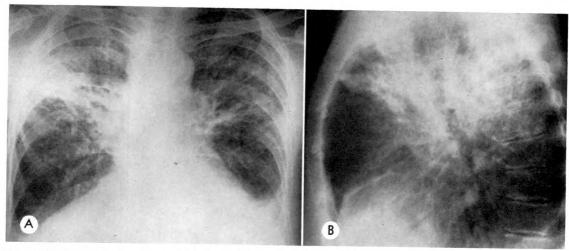


Fig. 3. Patient A.P., female, aged 76 years. Congestive cardiac failure due to aortic valve disease.

(A) Anteroposterior ward unit roentgenogram shows bilateral pulmonary edema in both mid and upper zones, more marked on the right than on the left. Small effusions are present at both bases. (B) Lateral roentgenogram shows some central distribution of the edema, but the upper lobe on the right side is mainly affected.

the edema was mainly basal. Two patients had mainly interstitial pulmonary edema (Table IV; and Fig. 4, A–D).

Unilateral and Shifting Edema. Three of 6 patients in this group had unilateral edema of differing segmental distribution (Fig. 5, A and B). In one of these the edema occurred at the time of angiocardiography and was apparently related to posture.

Report of a case. S.T. was a 6 year old male with a diagnosis of congenital mitral incompetence and coarctation of the aorta. He was found to have congenital mitral incompetence on a routine examination of the heart after discovery of the same abnormality in a sibling. Two years later, he began to tire easily and had frequent colds. Recently, he had been in frank heart failure and required digitalization.

Examination showed a pale small boy, who was not cyanosed. The heart was enlarged. His electrocardiogram demonstrated biventricular rhythm.

Cardiac catheterization revealed the following pressure data: pulmonary artery, 60/12; right ventricle, 62/0/7; right atrium, mean 3; left ventricle, 175/0/27; aorta 175/50; pulmonary wedge, mean 32. The cardiac output was 2.4 l./min. and the pulmonary arteriolar resistance 1.7 units.

Left ventricular angiocardiography showed

severe mitral incompetence with a mobile mitral valve and a large left ventricle. There was a gradient in the aorta noted on withdrawal of the catheter.

The blood pressure was: aorta, 175/50; brachial artery 149/50; and femoral artery, 112/62.

After the angiocardiographic examination, the patient was turned onto his right side by the anesthetist prior to removal of the endotracheal tube, and in this position he developed acute pulmonary edema in the right mid-zone. This was noticed on fluoroscopy of the chest and confirmed by a roentgenogram. The edema cleared rapidly after the patient was turned onto his back (Fig. 6, \mathcal{A} and \mathcal{B}).

In the remaining 3 patients, the edema appeared to shift freely from one lung to the other; that is, it cleared on one side and appeared on the opposite side. This was probably related to a change in posture. The exact distribution of the edema and the time relation of the shift are detailed in Table v (Fig. 7, A, B and C).

Summary of Results. Of the 20 patients studied, only I had intra-alveolar edema alone, 2 had interstitial edema alone, whereas in 17 both types of edema were probably present together (Fig. 8).

Pleural effusion or pulmonary infarction was an accompanying feature in several

cases, yet another factor complicating interpretation. Three patients had significant pleural effusion and 2 had evidence of pulmonary infarction.

DISCUSSION

The interpretation of the appearances and distribution of pulmonary edema, particularly the classic "batswing" shadows^{17,18} must be reconsidered in view of the analysis

of our cases. The classic "batswing" shadows as described by some authors was present in only 6 of the 20 cases in our study. Our findings on the lateral roent-genograms show that pulmonary edema is rarely of a purely central distribution. Any lung segment or combination of lung segments, central or peripheral, may be involved. The edema can be basal or apical, anterior or posterior, unilateral or bilateral,

TABLE IV
BILATERAL BUT NOT CLASSIC "BATSWING" EDEMA

Patient 1	Diagnosis	Bilateral Distribution	Intra-alveo <mark>l</mark> Additional Lui	Interstitial				
	9	Distribution	Right Lung	Left Lung	- Edema			
W.W.	Cardiac	Equal, then L>R	Superior segment lower lobe and posterior segment upper lobe	Superior segment lower lobe	Slight (P.H.H.; cuffing)			
A.M.	Cardiac	R>L	Superior segment lower lobe and pos- terior segment upper lobe		Slight (P.H.H.; cuffing)			
J.E.	Renal	R>L	Anterior segment upper lobe Apical posterior upper lobe Posterior and lateral basal segments lower lobe	Lower lobe	Marked (P.H.H.; S.L.; cuffing)			
E.C.	Cardiac	Equal but basal	Lower lobe	Lower lobe	Slight (P.H.H.; cuffing)			
N.S-J.	Cardiac	Central equal			Severe, mainly inter stitial (P.H.H.; cuffing; S.L.)			
A.S.	Renal	Central equal			Severe, mainly inter stitial (P.H.H.; cuffing; S.L.)			
F.J.	Cardiac	L>R		Anterior segment upper lobe	Slight (P.H.H.; cuffing; S.L.)			
P.B.	Renal	R>L	Lower lobe and medial segment middle lobe	Posterior basal lower lobe; lingula	Moderate (P.H.H.; cuffing)			

P.H.H. = Perihilar haze Cuffing = Peribronchial Perivascular cuffing

S.L. = Septal lines

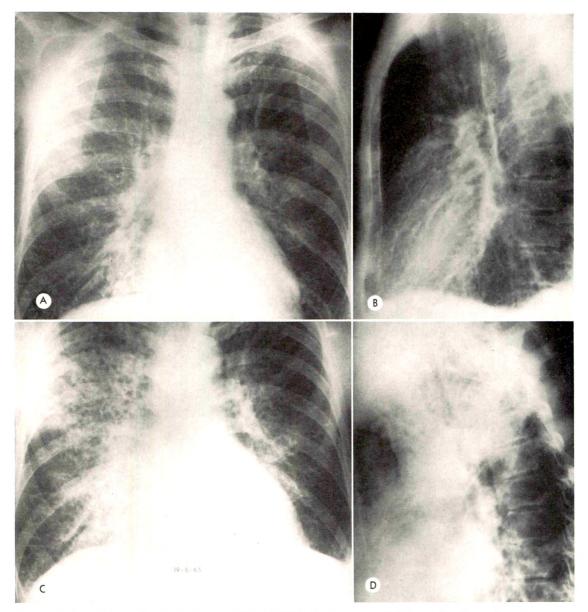


Fig. 4. Patient J.E., male, aged 56 years. Membranous glomerular nephritis, nephrotic syndrome.

(A, August 18, 1965) Anteroposterior ward unit roentgenogram shows marked edema of the right lung, mainly interstitial, well marked septal lines at the base and right perihilar clouding. (B) Lateral roentgenogram. There is no evidence of intra-alveolar central edema. Small basal effusion is present posteriorly.

(C) Anteroposterior ward unit roentgenogram a day later. In addition to the extensive interstitial edema, there is now evidence of some intra-alveolar edema in the mid and right upper zones and in the left mid zone. (D) Lateral roentgenogram shows that the edema is central and anterior, involving the upper, middle and lower lobes. The apical and posterior segments of the lower lobes are clear.

and can, in fact, shift very easily from area to area, segment to segment, or even appear to clear in one lung and reappear in the other. Analysis of serial roentgenograms from day to day, or even during an interval of hours, can show a remarkable change, not only in the extent or predominant type of edema, but also of its distribution.

Without lateral roentgenograms, localization of intra-alveolar edema is impossible. Intra-alveolar pulmonary edema accumu-

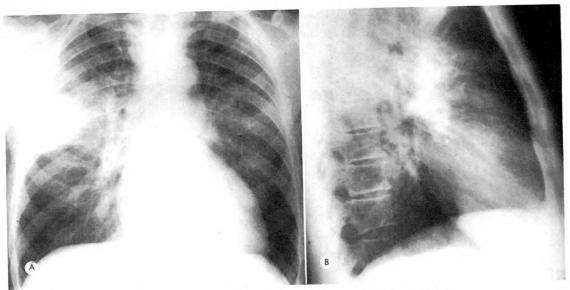


Fig. 5. Patient N.T., male, aged 63 years. Ischemic heart disease. Cardiac infarction.

(A) Posteroanterior full distance roentgenogram shows consolidation in the right upper lobe due to localized edema. (B) Distribution of the edema is central and posterior. The left lung is quite clear.

lating in the apical and superior segments of the lower lobe may appear as central edema, as may anterior or posterior segmental edema in the upper lobes.

Although we were unable to obtain a definite correlation between the distribution of pulmonary edema and posture or gravity, these two factors may have influenced the distribution in some instances.

This would explain the rapidly shifting fluid from lobe to lobe and even side to side, as was noticed in some of our patients. Posture was certainly of importance in patient S.T., who developed acute pulmonary edema while in the lateral decubitus position.

Another factor which probably affects the distribution of pulmonary edema is the

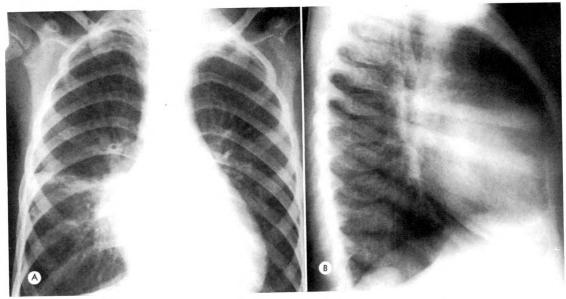


Fig. 6. Patient S.T. (A and B) There is evidence of pulmonary edema localized to the right middle lobe.

TABLE V
UNILATERAL AND SHIFTING EDEMA

Patient	Diag- nosis	Unilateral and Shifting	Intra-alveola Additional Lun	Interstitial Edema				
	110818	Distribution	Right Lung	Left Lung	Edema			
N.T.	Cardiac	Right	Posterior and anterior upper lobes	· •				
H.B.	Cardiac	Left		Superior segment lower lobe				
S.T.	Cardiac	Right	Middle lobe	Middle lobe				
N.C.	Renal	Left March 26, 1963		Lower lobe				
		Right March 29, 1963	Posterior upper and lower lobes	Slight residual				
A.H.	Renal	Bilateral Central May 30, 1963		Central	Moderate (S.L.; P.H.H.; cuffing)			
		Left April 2, 1963		Anterior segment upper lobe				
T.N.	Renal	Bilateral February 24, 1963	Upper lobe	Upper lobe	Moderate (cuffing; S.L.)			
		Left February 23, 1965		Lower lobe				

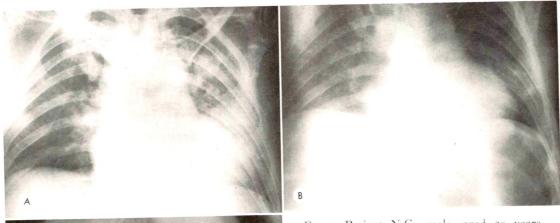
P.H.H.=Perihilar haze
Cuffing=Peribronchial
Perivascular
S.L. = Septal lines

variation in the pulmonary venous pressure associated with left heart failure. Hydrostatic differences of the pulmonary venous pressure due to change in posture may also influence its location and so may the deviation of pulmonary blood flow through the lungs from the lower zones to the upper zones in mitral heart disease and left sided heart failure.^{6,9,25}

A roentgenologic differentiation of interstitial and intra-alveolar edema on the basis of currently accepted criteria is not easy. The two types of edema are nearly always present together and some of the features can be easily confused. The perihilar haze of interstitial pulmonary edema or "hilar clouding" can be very similar to the shadows of centrally distributed intra-

alveolar pulmonary edema.^{17,18} It appears from our studies that in nearly all cases with intra-alveolar edema there is also evidence of interstitial pulmonary edema, irrespective of the underlying cause.¹⁴ There are certain roentgenologic features which are specific for interstitial pulmonary edema, such as septal lines and peribronchial and perivascular cuffing, and there are others, such as perihilar haze, which can be rather similar to the appearances of intra-alveolar pulmonary edema.

Although the appearances of septal lines (Kerley's A and B lines) are quite specific for interstitial pulmonary edema, the so-called perihilar haze and peribronchial and perivascular cuffing, also manifestations of interstitial pulmonary edema, may be



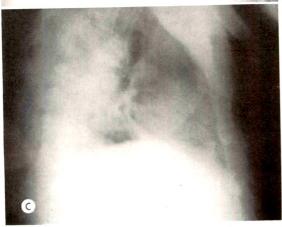


Fig. 7. Patient N.C., male, aged 39 years.
Malignant hypertension and chronic renal

(A, March 26, 1965) Anteroposterior ward unit roentgenogram shows extensive edema in the left lung, in the upper and lower zones and very slight edema in the right mid zone. (B) Anteroposterior supine roentgenogram taken 3 days later. The edema in the left lung cleared, but there is now a faint generalized haze over the right lung. (C) Lateral roentgenogram shows extensive edema posteriorly in the upper and lower lobes.

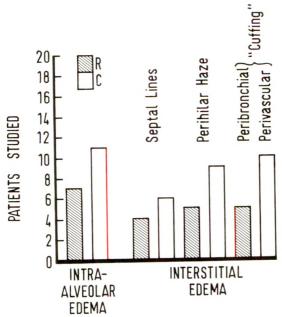


Fig. 8. Histogram showing the incidence of intra-alveolar and interstitial edema in the patients examined. R=renal cases; C=cardiac cases.

visible even before septal lines are obvious, as shown in some patients in the present study. This cuffing of end-on bronchi and arteries appears to be a useful and early sign of interstitial pulmonary edema.

Our analysis of roentgenologic appearances suggests that pulmonary edema due to cardiac disease and edema associated with a grossly elevated blood urea are very similar. In the majority of patients, cardiac failure was accompanied by a slightly elevated blood urea and the significance of this is uncertain. By the same token, some of the patients with primary renal failure also had evidence of cardiac failure.

The present study does not help to elucidate the mechanism of pulmonary edema, since in most of our cases multiple factors were operative, the two most important being cardiac failure, with an elevated pulmonary venous pressure^{9,12} and uremia, probably affecting capillary permeability.⁷

Hemodynamic studies by Finlayson et al.10 on 5 patients with pulmonary edema due to heart failure confirmed a high pulmonary venous pressure in 4 cases. These patients also had an elevated pulmonary arterial pressure which dropped after the clearance of the pulmonary edema. A correlation between an elevated pulmonary venous and pulmonary arterial pressure with the appearance of interstitial pulmonary edema in patients with left sided heart failure has been noted by others. 12,18,20 A high pulmonary venous pressure causing interstitial edema may be of greater importance than altered capillary permeability or the suggestion of a difference in the pulmonary arterial branching in the central medulla of the lung as compared with the peripheral cortex.16

SUMMARY

- 1. Lateral roentgenograms demonstrate that the edema which appears central on the frontal roentgenogram may, in fact, lie in anterior or posterior segments of any lobe of the lung.
- 2. Interstitial and intra-alveolar pulmonary edema accompany each other in most patients irrespective of the cause.
- 3. There are specific signs of interstitial edema, such as septal lines and peribronchial and perivascular cuffing, but others, such as perihilar haze, can be confused with intra-alveolar edema.
- 4. Although gravity probably plays a part in the distribution of edema, it is difficult to obtain conclusive evidence of this in all cases.
- 5. Pulmonary edema appears to shift easily and rapidly from lobe to lobe and from one lung to the other.

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ACUTE INTERSTITIAL PULMONARY EDEMA*

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THE pathologic division of pulmonary edema into intra-alveolar and interstitial types is well established.16 These two types may occur separately but more commonly occur in combination. The roentgen pattern produced by the intra-alveolar accumulation of fluid is well known, although the mechanisms producing its occasional peculiar batswing or unilateral distribution are not clear. 1,2,3,17 On the other hand, interstitial pulmonary edema is less often recognized, despite its common occurrence. Its roentgenographic appearance is quite different from its alveolar counterpart. The accumulation of edema fluid in the connective tissue framework of the lung is most often associated with mitral stenosis but may also be seen in long-standing left heart failure from any cause.11

The acute form of interstitial pulmonary edema is rarely mentioned in the literature. Since it characteristically produces no auscultatory findings, the correct clinical diagnosis is frequently a difficult one. Consequently, accurate evaluation of the chest roentgenogram is often the only means of diagnosis. The purpose of the authors is to summarize the salient roentgenologic features of this entity, to differentiate it from "alveolar" pulmonary processes and to emphasize the high frequency of its occurrence.

ROENTGEN FINDINGS

The roentgenographic features of interstitial pulmonary edema have been concisely outlined by Grainger⁸ as follows: (1) "A" and "B" lines of Kerley; (2) subpleural edema; and (3) hilar haze. In addition, a diffuse reticular pattern may be seen at times (Fig. 1 through 8).

"A" lines are linear, centrally placed, fine dense lines, up to 4 cm. in length, most frequently seen in the upper lobes di-

rected toward the hilus. Their pathologic origin and their site of predilection are variously interpreted. Grainger8 believes that they are due to edematous septal plates between pulmonary lobules. Trapnell²⁵ suggests that they represent markedly distended anastomotic lymphatic channels between the hilus and the pleura. accompanied by perilymphatic edema. "A" lines are known to develop secondary to pneumoconiosis,23 sarcoidosis,24 and malignant cell invasion.20 "A" lines have been reported in acute interstitial pulmonary edema²⁰ and were seen almost universally in our patients with this condition. Although "A" lines do occur from other causes, their very high incidence in acute interstitial edema should, when they are present, make this diagnosis the paramount consideration.

Kerley's "B" lines are fine, dense parallel lines, 1.5 to 2 cm. in length, most frequently seen in the lateral portion of the lung bases. Pathologically, they have been shown to represent thickened interlobular septa. The thickening may be due to fibrosis, pigment deposition or to deposits of abnormal cells as in sarcoidosis or malignancy. In most instances, the finding is transient and, therefore, probably due to edema fluid.

Another roentgen manifestation of interstitial edema is the apparent thickening of the pleura, especially in the interlobar fissures. This is actually due to subpleural edema, which extends in continuity from the subpleural interlobular septa and is difficult to distinguish from interlobar pleural fluid.

The term "hilar haze" has been used to indicate a loss of sharp definition of the large central pulmonary vessels. Short¹² postulated that this appearance was the result of interstitial accumulation of fluid around these vessels. Nonetheless, central alveolar edema has produced this finding,

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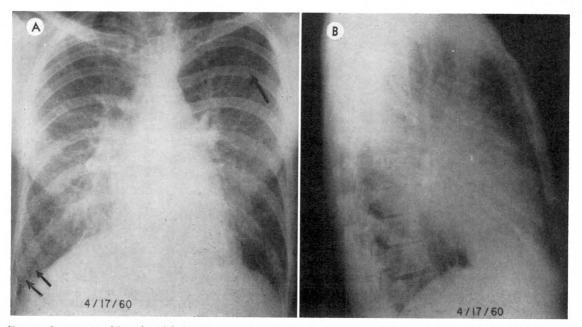


Fig. 1. A 29 year old male with known mitral stenosis admitted for evaluation of hematuria. There were no pulmonary symptoms or abnormal physical findings in the chest. (A and B) Prominent A-lines (\(\sigma \)) and B-lines (\(\sigma \sigma \)) are shown, accompanied by striking perihilar haze. There is a band of increased density related to one of the major fissures, apparently due to subpleural edema.

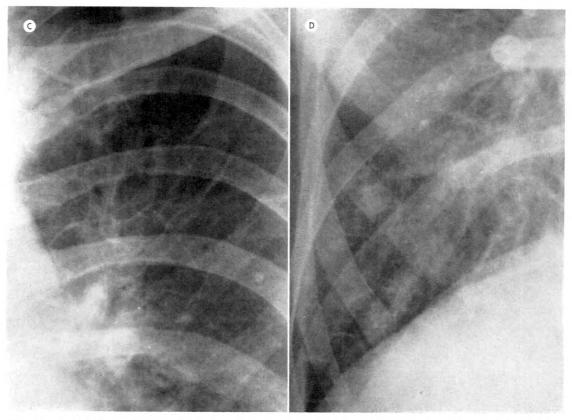


Fig. 1. (C) Detail of left upper lung demonstrates A-lines. (D) Detail of right lower lung shows B-lines.

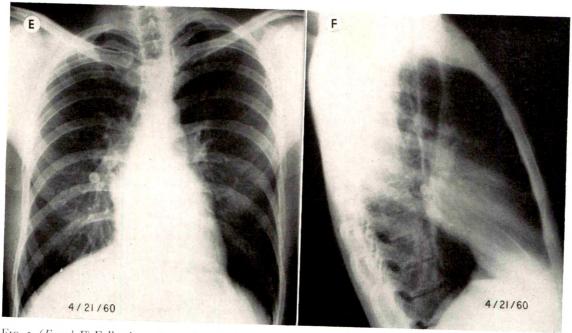


Fig. 1. (E and F) Following 4 days of medical management, the re-examination of the chest shows complete clearing of the findings indicative of interstitial edema. Comment. This case demonstrates some of the typical findings of acute interstitial pulmonary edema. It further demonstrates that despite no significant symptoms or physical findings, pulmonary edema was present and was detected only by roentgenographic study. Also demonstrated is the rapidity of clearing of the roentgenographic findings following the institution of proper therapy.

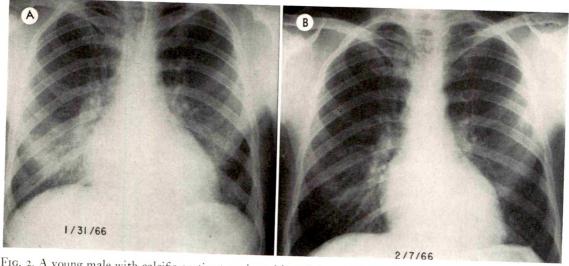


Fig. 2. A young male with calcific aortic stenosis and insufficiency. The patient was mildly dyspneic but no physical findings were present in the chest. (A) The admission roentgenogram shows diffuse perihilar haze without other roentgen findings of interstitial pulmonary edema. (B) A roentgenogram made after digitalization shows complete clearing of the perihilar haze. Comment. This case emphasizes hilar haze as a manifestation of interstitial pulmonary edema.

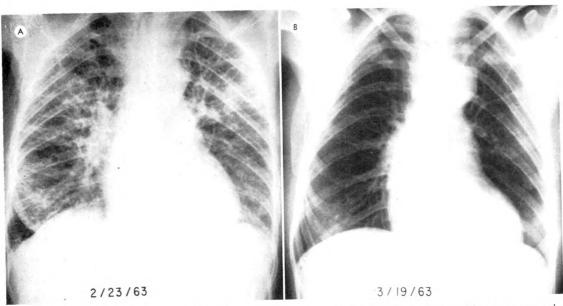


Fig. 3. Hyperthyroid female admitted with cough. There were scattered rales and rhonchi present over the lung fields. (A) There is a poorly defined diffuse reticular pattern accompanied by A and B-lines indicating interstitial abnormality. The over-all pattern probably is produced in part by distention of pulmonary veins; but there is, in addition, edema distending interstitial spaces producing the reticular pattern. (B) A roentgenogram made approximately 3 weeks after treatment for cardiac failure and hyperthyroidism shows complete clearing of the pulmonary abnormalities. Comment. This case emphasizes that a reticular pattern can be a manifestation of acute interstitial pulmonary edema.

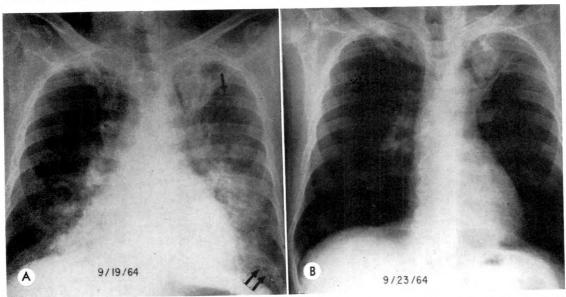


Fig. 4. A 62 year old male with bronchogenic carcinoma of the left upper lobe. The patient was admitted for acute onset of shortness of breath with moist rales, typical of pulmonary edema heard in the basal portions of the lungs. (A) The findings are those of a combination of alveolar edema and interstitial edema. The alveolar process is indicated by the dense fluffy perihilar opacities extending into the lower lobes, tending to be poorly outlined and to be coalescent. The presence of A-lines (A) and B-lines (A) indicates acute pulmonary edema of an interstitial type. (B) Following the institution of therapy, there is complete clearing of both the alveolar and interstitial processes. Comment. This case points out the common association of alveolar and interstitial pulmonary edema but emphasizes the findings which, in some cases,

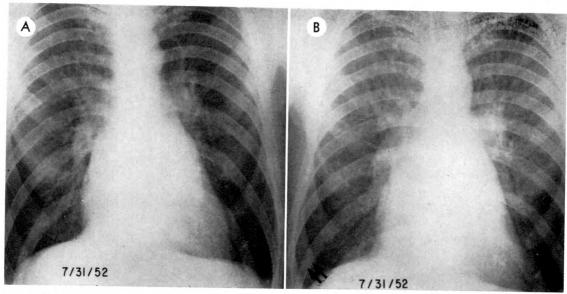


Fig. 5. Male with known mitral stenosis. (A) Posteroanterior chest roentgenogram demonstrates an enlarged left atrium with distention of upper lobe veins and contraction of lower lobe veins. (B) This patient was exercised and roentgen findings of interstitial pulmonary edema in the form of A-lines (A) and B-lines (A) are noted on the roentgenogram made immediately after exercise. In addition, there is greater distention of upper lobe veins. Comment. This case demonstrates graphically that A-lines and B-lines may develop in an extremely brief period of time as a manifestation of interstitial pulmonary edema. Such changes are apparently secondary to a rise in the pulmonary venous pressure to greater than 25 mm. of mercury. In this patient, the elevated venous pressure is graphically demonstrated by the distention of the upper lobe veins and the contraction of the lower lobe veins. Often, however, the abnormalities of veins are difficult to appreciate and when there is a rise in postcapillary pulmonary resistance, this frequently may be diagnosed roentgenographically with greater certainty from the findings indicative of interstitial pulmonary edema.

Kerley²⁰ believed that this sign was not due to pulmonary edema *per se* and implicated acute swelling of the hilar lymph nodes in the development of this pattern.

Kerley²⁰ has also described "C" lines, which he indicated to be very fine "spiderwed lines" covering most of both lung fields. It was his opinion that "C" lines probably represented distended pleural lymphatics. A diffuse reticular pattern, usually coarse but sometimes fine, has been emphasized as a manifestation of interstitial processes by Rigler.¹⁸ This reticular pattern and Kerley's "C" lines may be identical, although to our knowledge "C" lines have not had pathologic verification. A coarse

reticular pattern as a manifestation of acute interstitial pulmonary edema has been seen in our material (Fig. 34).

When the roentgenographic manifestations of interstitial pulmonary edema develop, the condition may progress rapidly to frank alveolar edema. Sometimes, however, the pattern of interstitial edema arising acutely may show persistence of this roentgenographic appearance for periods of weeks or months.

The roentgen picture is occasionally bizarre and may mimic interstitial fibrosis (Fig. 3A). However, the presence of an interstitial pattern in an acutely dyspneic person should strongly suggest the diagno-

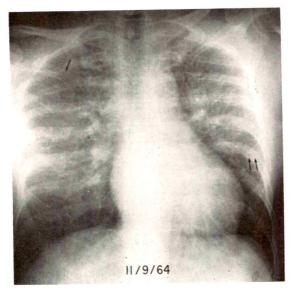


Fig. 6. A 50 year old female with an acute myocardial infarction. Although moderately dyspneic, she demonstrated no abnormal physical findings in the chest. A supine roentgenogram of the chest made 2 to 3 hours after infarction indicates a poorly defined central pulmonary haze with many A-lines (/) and occasional B-lines (//). The patient expired 2 hours after the roentgenogram was made. An autopsy showed findings of acute interstitial and alveolar pulmonary edema. Comment. This case again demonstrates that interstitial pulmonary edema may develop acutely. In this case, the interstitial pulmonary edema was combined with alveolar edema at the time of death. In the absence of abnormal physical findings, the diagnosis of pulmonary edema was made solely on roentgenographic grounds but was made with certainty because of the roentgenographic evidence of an interstitial process which had developed in an acute clinical situation.

sis of acute interstitial pulmonary edema. Although rarely an interstitial pattern has been reported to develop acutely with viral infections and with farmer's lung, such a pattern which develops or resolves rapidly is very likely due to interstitial pulmonary edema, especially when "A" lines are present.

DISCUSSION OF ETIOLOGY

In the lungs of normal individuals, transudation of fluid into the interstitial spaces is minimal, due to the relatively low vascular filtration pressure and the higher plasma

osmotic pressure. Transudation will result, however, under the following circumstances: (1) Increased pulmonary filtration pressure due to altered flow or resistance; (2) decreased capillary osmotic pressure; and (3) increased capillary permeability.

The barrier normally separating the plasma within the capillaries from the alveolar spaces is extremely thin (about 0.8 µ) and is composed of capillary endothelium, interstitial tissue, alveolar lining membrane and the mucin layer lining the alveolar space. 15 If edema collects in this potential space between the capillary basement membrane and the alveolar basement membrane, the pulmonary lymphatics attempt to remove it. Experimental occlusion of pulmonary veins causes increased flow from pulmonary lymphatics.26 If the edema fluid collects too rapidly to be removed by available lymphatics, it may leak into the air passages, producing the classic signs of frank pulmonary edema. In some instances, however, the transudate may not pass immediately into the alveolar space, but may remain in the interstitial region. This then makes the lungs more rigid, gaseous exchange is impeded and dyspnea may occur, often in the absence of rales and other physical findings. Occasionally, however, patients with acute interstitial edema may be asymptomatic with only the roentgen findings as a warning of impending disaster (Fig. 1, A–F; and 3, A and B).

Interstitial pulmonary edema of cardiac origin results most commonly from those conditions (disease of the left ventricle, mitral valve, left atrium and occasionally the pulmonary veins) in which there is an increase in postcapillary resistance followed by an increased venous pressure greater than 25 mm. of mercury. 19 In mitral stenosis or chronic left ventricular failure, the transudation of fluid into the alveolar spaces is hindered by an increased thickness, often up to 15 μ , that occurs in the alveolar wall and adjacent connective tissue. 16 In these diseases, the transudate is apparently arrested and held in this expanded interstitial space. This explains the

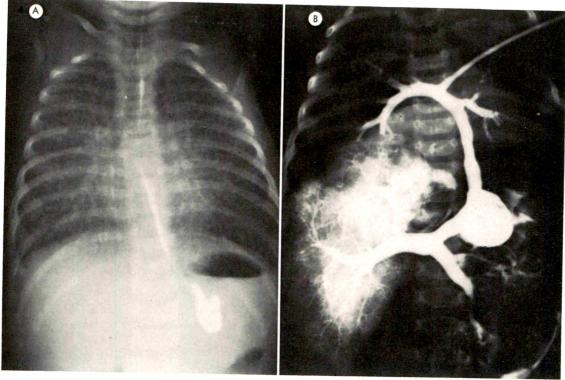


Fig. 7. Female with total anomalous pulmonary venous return into the portal system. (A) Posteroanterior chest roentgenogram shows irregular linear and reticular densities distributed uniformly throughout the lungs with the probable presence of B-lines at the right base. (B) Postmortem injection shows drainage of pulmonary veins into the sinus venosus. Comment. This case suggests that the pulmonary shadows seen in patients with anomalous pulmonary venous return with obstruction represent interstitial pulmonary edema secondary to the elevation of postcapillary pulmonary resistance. This may develop acutely with the commencement of pulmonary blood flow at birth but can progress to a subacute or chronic state. Although dyspneic, these patients usually do not show physical findings in the chest.

common occurrence of chronic interstitial pulmonary edema in these entities. On the contrary, why interstitial localization of edema fluid should be seen in some cases of acute cardiac failure and not in others is not known. In all likelihood, it is dependent on the degree and/or rapidity of increase in pulmonary venous pressure.

It would seem that "A" lines developing from cardiac causes tend to appear with a sudden rise in venous pressure to a high level. Thus, in Carmichael and co-workers's series, "A" lines were observed in cardiac patients with the highest pulmonary-capillary pressures, which roughly reflect the pulmonary-venous pressures. In contrast, in Short's²¹ series of patients with interstitial edema secondary to chronic left ventricular failure, no case demonstrated "A"

lines. Their absence was probably due to either a slow development of the interstitial edema, or to the relatively low venous pressure. Why the "A" lines are seen selectively in the upper portions of the lungs is not clear, unless this phenomenon is related to the presence of a greater number of deep pulmonary lymphatics in this area, as suggested by Trapnell.²⁵

SUMMARY

Interstitial pulmonary edema is more common than is generally appreciated. Heretofore, it has been recognized almost always in association with chronic left ventricular failure or with mitral stenosis. Nevertheless, acute interstitial pulmonary edema does occur not infrequently in a variety of other clinical conditions. Such

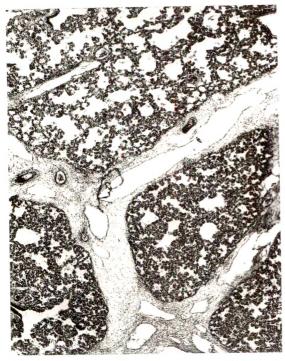


Fig. 8. Photomicrograph (×38) of lung from a patient with relative pulmonary venous obstruction secondary to total anomalous pulmonary venous return. The marked edema of the interstitial space is clearly shown.

patients may be asymptomatic or markedly dyspneic, but frequently do not manifest physical findings of pulmonary edema. Consequently, the diagnosis becomes a roentgenographic one. The roentgen picture may mimic interstitial pulmonary fibrosis. However, the presence of an interstitial pattern in an acutely dyspneic person or an interstitial pattern which develops or clears rapidly should strongly suggest the diagnosis of acute interstitial pulmonary edema. The presence of "A" lines should support a diagnosis of acute interstitial pulmonary edema, since they occur in very high incidence in this condition and much less frequently in interstitial processes of other origin.

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THE ROENTGEN FEATURES OF EATON AGENT PNEUMONIA

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FEW reports have appeared in the literature in recent years about the roent-genographic findings in Eaton agent pneumonia. Much work has been done, however, on the mycoplasma organisms and their role as pathogens in human disease. The history of this work was succinctly reviewed by Shepard and Calvy⁷ and will be briefly alluded to further on.

The purpose of the author is to discuss the chest roentgenographic findings in a series of 38 patients diagnosed at U.S. Army Hospital, Würzburg, Germany, from January 1,1965 to January 1,1966. In all instances the patients included in the study displayed typical clinical findings, had high titers of cold agglutinins in the serum and had pulmonary infiltrates in the lungs proven by roentgenograms.

The liberal utilization of the cold agglutinin determination in patients with pulmonary infiltrations uncovered a high percentage of Eaton agent infections at our hospital. In a rather select group of military personnel and their dependents, an estimated 25 to 50 per cent of patients hospitalized with pneumonia were found to have Eaton agent infection. This experience is consistent with that of Chanock et al., who studied marine recruits at Parris Island and found that a large percentage of patients with severe lower respiratory tract illness during the interval of their study had Eaton agent infection.

HISTORY

Eaton agent pneumonia, more commonly refered to as primary atypical pneumonia in the past, is a specific disease caused by the bacterium, *Mycoplasma pneumoniae*. This organism was first identified as a cause of pneumonia by Eaton *et al.*, in

1944. Proof that it caused human infection was demonstrated with the fluorescent antibody technique by Liu in 1957. In recent years, studies in military personnel have established a major role for the Eaton agent in the causation of upper and lower respiratory tract infection.^{2,6}

In this series of patients, the fluorescent antibody test was not used as the cold hemagglutinin test is far simpler and more practical. Though not specific, this test is strongly positive in Eaton agent pneumonia. It has been found that about 90 per cent of cold agglutinin producing infections are due to the Eaton agent.4 Low titers are encountered in a variety of diseases such as rubella, infectious mononucleosis, catarrhal jaundice, hemolytic anemias and influenza.8 Of these, only influenza enters into the differential diagnosis and this diagnosis was considered to be excluded in the cases included in this series. In many instances, exceedingly high titers of cold agglutinins, seen only in Eaton agent infection, were obtained.

CLINICAL FINDINGS

The typical case in which there is pneumonia has a prolonged 3 to 6 week course. There is high fever, dry cough, headache, malaise, sore throat, and nonpleuritic chest pain. The white blood cell count is usually within normal limits and secondary bacterial infection is infrequent. The cold hemagglutinins are elevated during the course of the illness and reach levels of 1:32 or higher in about 80 per cent of the cases. In a series of 45 cases reported by Young, no relationship between titer and severity of illness could be demonstrated.

Of practical significance is the evidence to indicate that the broad spectrum anti-

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biotics are effective in the treatment of Eaton agent pneumonia, whereas penicillin and sulfa drugs are of doubtful value.⁵

Pulmonary infiltration of varying degree is a prominent feature of Eaton agent infection. It should be appreciated, however, that there are many such infections which are not associated with elevated hemagglutinins or with pulmonary infiltration. Included in the series reported here are 2 siblings of a family comprising 5 individuals. These 2 children had Eaton agent infection with pulmonary infiltration; the other members of the family all had elevated hemagglutinins with respiratory tract symptoms but no pulmonary infiltrations were demonstrated on roentgenograms of the chest.

MATERIAL

Thirty-eight cases of Eaton agent pneumonia were reviewed in order to establish any features which might be characteristic. There were 34 adults, mostly under 30 years of age, and 4 children with the disease.

From a clinical standpoint, the adult and childhood illnesses showed no differences. The cold hemagglutinin titers were 1:32 and often much higher and there was no correlation between titer and severity of illness. In almost all cases, response to treatment with broad spectrum antibiotics was good. It is quite possible that the infections might have cleared as rapidly without antibiotic therapy. In this healthy group of patients, there were no immediate complications of the illness and in only 2 individuals were the signs and symptoms of respiratory tract disease pronounced.

ROENTGENOGRAPHIC FINDINGS

Infiltration of the lungs was usually localized to one lobe of the lung. The infiltrate could best be described as patchy with the pulmonary vessels discernible within the infiltrate, and often with radiation from and confluence with the hilus (Fig. 1).

The infiltrate skipped from one area of the lung to another, usually adjacent, area

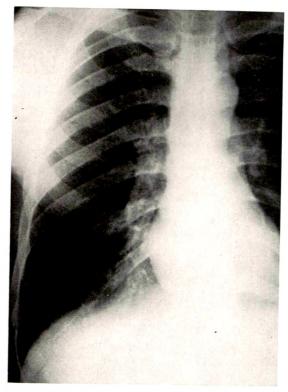


Fig. 1. Typical lower lobe infiltrate. Pulmonary vessels are discernible within the infiltrate. Despite a basilar location, all such infiltrates resolve without the slightest pleural reaction.

in 5 cases (13 per cent). In Figure 2, A, B and C is shown a case of upper lobe involvement with skip to the lower lobe. In all cases this skip phenomenon seemed to have no clinical significance.

Hilar lymphadenopathy was found in only 3 cases (8 per cent), but there was obscuration of the hilus by the infiltrate in 10 cases. Roentgenograms of the chest during the resolution phase of the process did not suggest any hilar enlargement in those cases where there had been obscuration earlier.

In not one instance of Eaton agent pneumonia was a pleural effusion detectable. This experience substantiates the reported rarity of pleural effusion in this disease. Two cases with elevated hemagglutinins over 1:32 and with pulmonary infiltration and pleural effusion had to be excluded from the series when a diagnosis of tuberculosis was subsequently made.

In 5 cases the pulmonary parenchymal

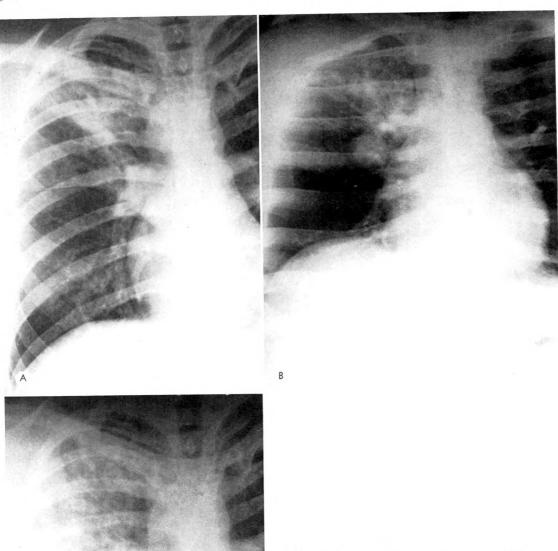


Fig. 2. (A) Upper lobe infiltrate. (B) Apical lordotic view taken on the same day demonstrates hilar lymphadenopathy. (C) Three days later, there is more pronounced involvement of the anterior segment of the upper lobe with skipping to the lower lobe as well.

infiltrate had a distinctly nodular and reticular appearance (Fig. 3 and 4). In all cases the densities were confined to one lung. This pattern should not be confused with the miliary or reticular pattern of granulomatous pneumonitis where the densities are smaller. Malignant metastatic nodules and lymphogenous metastatic infiltrations of the lung are easy to exclude since they are persistent, whereas the densities of Eaton agent pneumonitis are transient, seldom lasting longer than several days.

SUMMARY

The relatively high incidence of Eaton agent infection in military personnel and their dependents is probably the most striking revelation of this study.

Review of the roentgenograms of 34 young adults and 4 children with Eaton agent pneumonia revealed no characteristic diagnostic features. The pulmonary in-

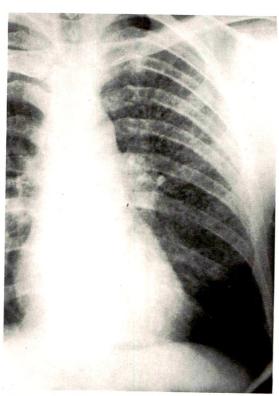


Fig. 3. Combined nodular and reticular infiltrate of the upper lung field.

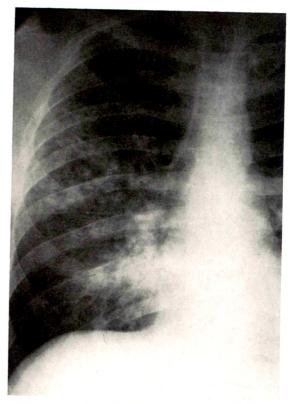


Fig. 4. Another nodular and reticular infiltrate persisting only a few days.

filtrate is bronchopneumonic in type and clears without residual pleural or parenchymal scarring. Hilar lymphadenopathy is not too common and pleural effusion is so rare as to suggest a different diagnosis.

Response to broad spectrum antibiotics was satisfactory and there were no complications. No biopsy or autopsy material was available for study.

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ROENTGENOGRAPHIC MANIFESTATIONS OF VARICELLA PNEUMONIA WITH POSTMORTEM CORRELATION*

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THICKENPOX is one of the common contagious diseases of childhood and is usually benign. In adults, it has not been generally appreciated that it may occasionally be accompanied by severe varicella pneumonia, with other associated complications, which may prove fatal. Probably the first American documentation of autopsy findings in systemic varicella was made by Johnson²² in 1940. He credits Schleussing with a report of neonatal varicella from Germany, dated 1927. Johnson observed focal necrosis in the skin, esophagus, pancreas, liver, renal pelvis, ureters, bladder and adrenals of a 7 month old child dying of the disease. Since that report, detailed case reports and small series have continued to document the findings in fatal cases.2,9,11,16,26,29,34,86,46

Chickenpox pneumonia is relatively rare in children. Krugman et al.²⁶ state that in the pediatric age group primary varicella pneumonia is rarely encountered. Pulmonary involvement has been described both in newborn infants⁵ and in children who have contracted chickenpox while on steroid therapy for another disease. It has been reported as an autopsy finding in infants with varicella neonatorum²⁹ and congenital chickenpox.²⁴ In general, however, pulmonary complications of varicella in childhood usually have a bacterial etiology, hemolytic Staphylococcus aureus being the most frequent offender.²⁶

The incidence of viral varicella pneumonia is estimated as between 1 to 8 per 1,000 cases of chickenpox.^{6,12,14,32} It is generally agreed that adults, although approxi-

mately 10 times less susceptible to varicella than children, are more prone to development of this specific complication of virus pneumonia.25 Varicella pneumonia has been reported to occur in as high as 16.5 per cent of all adults with varicella.47,48 Although primary varicella pneumonia is a clinical entity that has been described as a rare and severe disease in adults,20,88 many reports have been added to the literature since the first description in 1942 by Waring and his associates.46 It has been described in adults ranging from 17 to 71 years of age, 11,47 with a fatal outcome in 16 per cent of cases reported by Krugman et al. The roentgenographic features of chickenpox pneumonia were first described in 1942 by Waring, Neubuerger and Geever. 46 Thirteen additional detailed reports up to 1965 list approximately 152 cases. 7,8,9,18,24,80,81,85,89,40,

PATIENT MATERIAL (TABLE I)

Twenty patients with the diagnosis of primary varicella pneumonia have been admitted and treated at our hospital since 1960. Onset of symptoms occurred 3 to 7 days before hospital admission. Fever was always the first manifestation and was present in all cases, ranging from 102° F. to 106° F. Adults commonly complained of "chills" and aching in muscles and back. The typical varicella skin rash appeared on the second or third day and was very severe in all cases. Cough was present in all cases and hemoptysis and inspiratory chest pain were present in 7 cases (35 per cent). Dyspnea was present in 16 cases (80 per cent), 1

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Table I clinical and laboratory findings in 20 cases of primary varicella pneumonia

Nicholas Sargent, Merl J. Carson and Emmett D. Reilly																			
	Computations	Died after 9 hr. Midbrain hemorrhage. Cardiac	arrest. Died after 14 hr. Varicella pneumonia and hepa-	Died after 8 hr. Osteomyelitis, staphylococcal	Schus Died after 3 da. Hypogammaglobulinemia,	stupny lococcat sepsis Died after 26 hr. Varicella pneumonia and hepa-	Died after 4 hr. Viral encephalitis, cerebral edema,	necrosis of spicen and liver, bronchitis None	None	Thrombophlebitis	None	None	None	None	None	None	None	None	
Treatment	Ster- oid	0	+	0	+	0	0	+	0	+	0 0	·+	0	0 0	· +	0	+ '	0	-
Treat	Anti- biotics	+	+	+	+	+	+	+	+	+-	+ °	· +	+-	++	-+	+	+ '	0 0	
White Blood	Cell Count	13,600	12,500	∞9,6	6,900	20,100	19,000	19,400	9,800	16,300	6.100	8,18	8,80	×,3	6,800	5,950	15,400	7,38	
Chest Roentgeno-	grapnic Abnormalities	No roent-	genogram +++	+++	++++	+++	No roent-	genog am	+++	+ -	+ + + + + +	-+ + +	+-	+ + + + + +	-+ -+ -+	++	+- +- +-	 	
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Key: +++ severe; ++ moderate; + mild; o absent; N normal; D deceased.

to 2 days before admission, while cyanosis was observed only in 2 instances.

Physical examination on hospital admission revealed dyspnea in all but I case, with respirations from 20 to 90 per minute. A very severe varicella skin rash was universally present, also involving the mucosa of the mouth and pharynx. Body temperature was elevated in all but I patient with a maximum of 104.2° F. Cyanosis of skin and mucosa was obvious in 11 patients (55 per cent). One patient was disoriented and I was comatose. Examination of the lungs revealed rales in one or both lungs in II cases (55 per cent) with decreased breath sounds in 12. Six patients had no auscultatory evidence of pulmonary pathology, yet roentgenographic study revealed evidence of marked pneumonia of both lungs in each case.

Routine laboratory investigations revealed white blood cell counts of from 5,950 to 20,100 per cu. mm. with 13 cases under 10,000 per cu. mm. Differential white blood cell counts were normal in half of the cases with a slight to moderate left shift in the remainder. Blood culture was positive in only 2 children (hemolytic Staphylococcus aureus). One child had associated osteomyelitis and the other hypogammaglobulinemia with sepsis.

ROENTGENOGRAPHIC FINDINGS

Eighteen of the 20 patients reported in this study were found to have definite roentgenographic abnormalities in the lungs. Cases I and 6 died before chest roentgenograms could be obtained. Four of the 20 cases had moderate roentgenographic changes associated with moderate clinical findings. The remaining I4 had extensive roentgenographic findings, although 2 of these had mild clinical symptoms

As in all cases, although the roentgenographic findings differed in detail, they were generally similar enough to define a fairly characteristic pattern. Diffuse miliary or nodular patterns were seen throughout both lung fields. Although the nodules measured approximately 0.5 cm. in diameter, many were quite variable in size and were superimposed upon markedly increased bronchovascular markings. The nodules appeared to be separate and distinct from the surrounding tissues, especially in the thinner peripheral portions of the lung fields. Many of the nodules, however, did coalesce, particularly in the hilar and perihilar regions. The nodular alveolar infiltrates were actually acinar nodular lesions with fluffy, indistinct margins (Fig. I, \mathcal{A} and \mathcal{B}).

Transitory changes were common and the disease changed rapidly in several of the cases. Some areas of nodulation resolved, as other new areas appeared. With the tendency of some of the nodules to coalesce, there appeared to be patchy areas of consolidation (Fig. 2). This was especially true at the lung bases. No portion of the lungs was spared, although the densities appeared to be heavier in the perihilar regions, gradually diminishing towards the periphery (Fig. 3). In addition, the lung roots and the hilar shadows were increased in prominence and some actually did show a definite increase in size. Nodular hilar lymphadenopathy was present in 2 cases (Fig. 4, A and B), which subsided as the pulmonary infection resolved. The hilar lymphadenopathy was associated with generalized lymphadenopathy in these 2 cases.

Two cases showed blunting of the costophrenic angles associated with a minimal amount of fluid which cleared rapidly.

POSTMORTEM FINDINGS (TABLE II)

In six cases the outcome was fatal and the changes were studied pathologically. In all cases included in this series, the cutaneous lesion was the hallmark of the disease and all patients presented with severe involvement of the skin. Further, the visceral lesions found at autopsy resembled the skin effect, modified by the tissue response in the various areas. The various lesions seen on any given patient differed from each other in order of development and severity. Thus regularly there were papules, vesicles

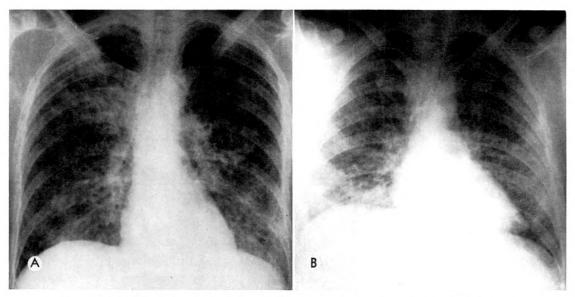


Fig. 1. (A and B) Typical cases of varicella pneumonia showing acinar nodular lesions.

and pustules simultaneously present on the same patient (Fig. 5). Microscopically, the earliest lesions consisted of congestion and edema of the corium. A local inflammatory infiltrate was present which included numerous monocytes and lymphocytes. More severe lesions showed cytoplasmic ballooning and nuclear pyknosis of epithelial elements. A continuation of this process resulted in the classic intra-epithelial vesicle

surrounded by necrotic epithelial elements. The most severe lesions produced necrosis of the entire thickness of epithelium including the dermis. The stromal inflammatory response was correspondingly greater and included many polymorphonuclear leukocytes. Secondary staphylococcal infection was a serious problem in 2 cases. Definite viral inclusion bodies were demonstrable in only 2 cases. Involvement of the dermis by



Fig. 2. Coalescent nodules with patchy areas of consolidation.

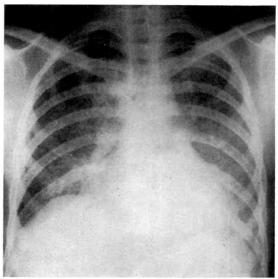


Fig. 3. Hilar involvement diminishing towards periphery of lung fields.

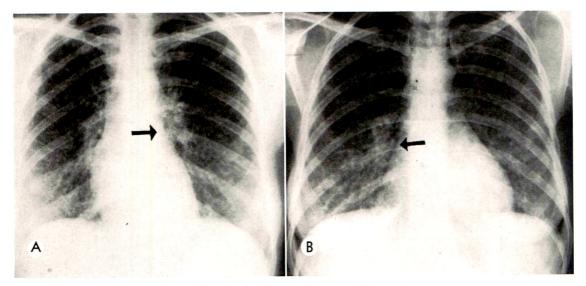


Fig. 4. (A and B) Nodular hilar lymphadenopathy.

the continuing process of necrosis resulted in damage to local vessels with consequent secondary hemorrhage into lesions. Thus, the over-all process in the skin was one of varying degrees of cellular necrosis, possibly related to continuing viral propagation. Specificity of epithelial involvement was only relative since even in the more severe skin lesions, connective tissue and vascular destruction could be observed. Although inclusion bodies in cutaneous vessels could not be demonstrated, they were occasionally discernible in the visceral vessels.

The visceral changes were similar to those noted in the skin. Focal areas of necrosis resembling the familiar cutaneous pox were seen in many areas and important secondary changes were present in many structures. The virus has an apparent avidity for mesothelium lined structures and, in all cases, the pleura and peritoneum were involved. In the peritoneum the lesions were often superficial. Thus, a serosal lesion on the gastrointestinal tract was usually not associated with a mucosal defect. In contrast, pleural, splenic, capsular and hepatic surface involvement was invariably associated with parenchymal destruction. Although the pleural or peritoneal lesion was itself covered by a layer of fibrin, generalized accumulations of fibrin or extensive amounts of free fluid were not observed.

The pulmonary changes seen included pleural, parenchymal, tracheobronchial and interstitial involvement. The pleura was marked by a series of localized, strikingly reddened, moderately elevated areas surrounded by a pale, blanched rim of tissue. Early vesicle formation appeared to be present in the center of the lesion (Fig. 6A). The lungs, which weighed 2 to 3 times normal, showed on cross section edema and hemorrhage, plus areas of confluent bronchopneumonia (Fig. 6B). The trachea and bronchi were markedly reddened and edematous. In some cases, pox were grossly visible within the trachea (Fig. 6C). In I case, an interstitial pneumothorax could be seen. Microscopically, the tracheobronchial lesion usually consisted of marked submucosal edema and hyperemia. A mixed inflammatory infiltrate including lymphocytes, reticulum cells and polymorphonuclear cells extended into and around the muscular layers and local glands. Occasionally, the covering respiratory epithelium had become destroyed, thus producing a small ulcer. Pulmonary parenchymal changes consisted of septal swelling occasioned by hyperemia as well as swelling of septal cellular elements. The alveoli were

Table II
POSTMORTEM DISTRIBUTION OF LESIONS BY ORGAN SYSTEM

Case	I	2	3	4	5	6
Skin	Face, chest, arms 4+	Head, neck, chest, thighs	Face, chest, arms 4+	Face, chest, arms, lower extremities 4+	Face, chest, back 4+, oral mucosa 4+	Trunk, arms, legs 4+
Musculo- Skeletal						
Respiratory	Pleural pox, pneumonia	Pleural pox, pul- monary edema, tracheal ulcera- tion, hemorrhagic pneumonia	Pleural pox, pneumonia	Pleural and tra- cheal pox, pul- monary infarc- tion, hyaline membrane, inter- stitial pneumo- thorax	Pleural pox, pneumonia	Pleural pox, tracheal pox, bronchitis, in- clusion bodies
Cardio- Vascular			Myocardial abscess			Epicardial pox
Hemic and Lymphatic		Septic spleen and necrosis, lymph node necrosis, marrow hyper- plastic	Splenic pox	Splenic capsular pox, reactive hyperplasia	Splenic pox, lymph node necrosis	Splenic necrosis and infarction, reactive hyper- plasia
Digestive	Peritoneum pox, liver pox	Esophagus pox, liver pox, necrosis of peritoneum	Liver pox, esophagus pox, peritoneum pox	Liver pox on capsule, areas of necrosis of peritoneum	Esophagus pox, liver	Liver subcapsu- lar necrosis, peritoneum
Urogenital		Left ovarian pox				
Endocrine						
Nervous System	Petechial mid- brain hemor- rhage			Cerebral edema, perivascular cuffing	Edema, micro- gliosis plus satellitosis	Perivascular lymph nodes, edema of brain and cord
Cause of Death		Varicella pneu- monia	Varicella pneu- monia, staphylo- coccal septicemia	Respiratory in- adequacy, cere- bral edema, vari- cella encephalitis		Cerebral edema, varicella enceph alitis

found to contain large amounts of precipitated protein which often was "plastered" against the alveolar wall, reminiscent of hyaline membrane disease. Active inflammatory cellular response was present, consisting of a mixture of mononuclear forms and polymorphonuclear cells. Prominent septal cells were frequently seen. Endothelial involvement with local areas of necrosis and hemorrhage lay beneath the pleural pox, but could also be found elsewhere (Fig. 7, A–D).

Cardiovascular changes were usually limited to endothelial and muscular swelling in small arteries and veins. Occasionally, this process had progressed to frank necrosis. Epicardial pox (Fig. 8) was not infrequently seen but usually was not associated with myocardial damage. In I case

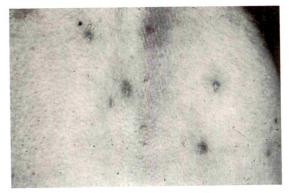


Fig. 5. Cutaneous varicella.



Fig. 6. (A) Pleural pox. (B) Pleural pox and hemorrhagic pneumonia. (C) Tracheal pox.





with secondary staphylococcal sepsis, a small subendocardial abscess was noted in the intraventricular septum.

The spleen and lymph nodes were invariably moderately enlarged due to reactive hyperplasia. The splenic capsule was usually the site of one or more pox accom-

panied by local areas of parenchymal necrosis. In none of the cases observed did a subcapsular hematoma or rupture result from the damage.

The oral mucosa contained pox in most cases. Pox involved the esophageal mucosa in 2 cases. Hyperemia and occasional pox

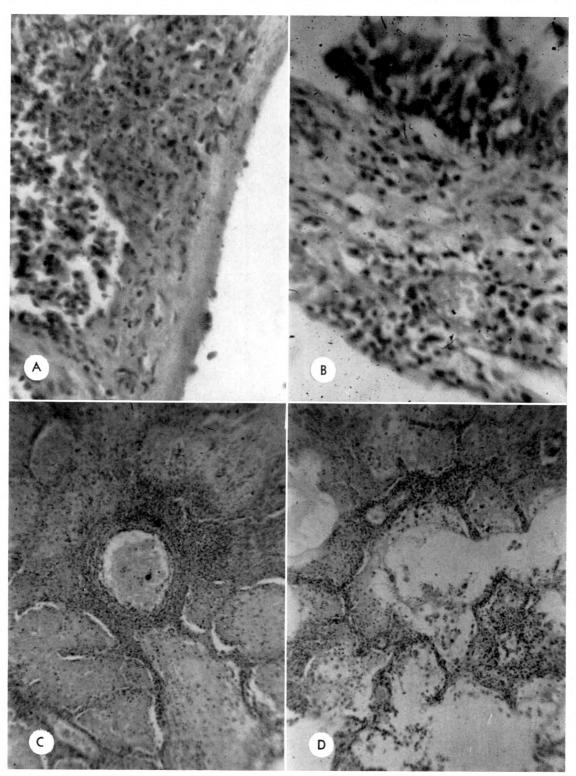


Fig. 7. Microscopic studies. (A) Pleural pox. (B) Acute bronchitis. (C) Pneumonia, vascular damage. (D) Pneumonia, pulmonary edema.

marked the serosa of the stomach and the small and large intestine in all cases, but mucosal involvement was not present. No pancreatic disease was found. The liver invariably showed serosal pox accompanied by local necrosis. Similar foci of necrosis were usually seen in the parenchyma and showed no predisposition for any portion of the lobule. Changes ranged from areas of cellular swelling with pyknosis to areas of frank necrosis infiltrated by polymorphonuclear leukocytes.

Necrotic lesions were not found in the kidney, and tubular swelling without necrosis was the only abnormality seen. In I case, a single ovarian pox was found.

Nervous system involvement was frequent. In half the cases, meningo-encephalitis with edema contributed to death. The meninges on gross examination showed only hyperemia or appeared normal. Microscopically, the subarachnoid space contained accumulations of lymphocytes, histiocytes and rare polymorphonuclears. Sections through the brain and spinal cord showed striking edema. Occasional perivascular lymphocytic cuffing was noted. Attempts to isolate virus from 3 of the cases were uniformly unsuccessful.

DISCUSSION

In reviewing our 20 cases, the pattern described by Southard⁴⁰ follows a similar pattern of epidemiology. The symptoms, signs, laboratory studies and pathologic and roentgenographic findings are also in a similar pattern. A typical course in the adult case may be reconstructed as follows:

An adult patient develops chickenpox 2 weeks after caring for a child who had the disease. There is no history of previous chickenpox disease. Fever is followed within 48 hours by a skin rash and a dry harassing cough develops. The rash rapidly involves the oropharyngeal mucosa. The cough becomes productive of tenacious blood-tinged sputum with onset of chest pain, dyspnea and cyanosis. Hospital admission reveals the patient to be acutely ill with fever, tachycardia and tachypnea.

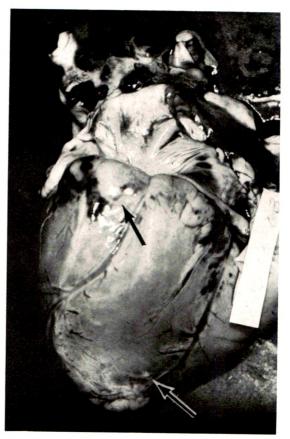


Fig. 8. Epicardial pox.

Sputum and blood cultures reveal no pathogens and all agglutination studies are negative. The white blood cell count is normal without significant left shift of the differential count. Admission chest roentgenograms reveal diffuse areas of fine, nodular infiltrations throughout both lung fields with a tendency towards confluency. Despite oxygen, supportive therapy and wide spectrum antibiotics, improvement is by lysis. A roentgenogram of the chest 7 days after admission shows some clearing of the miliary pulmonary infiltration with further clearing by the 10th hospital day. One month later, the patient is symptom free and no significant abnormality is noted on the pulmonary roentgenogram. This picture seen in adults is in sharp contrast to the usually mild course of childhood chickenpox.

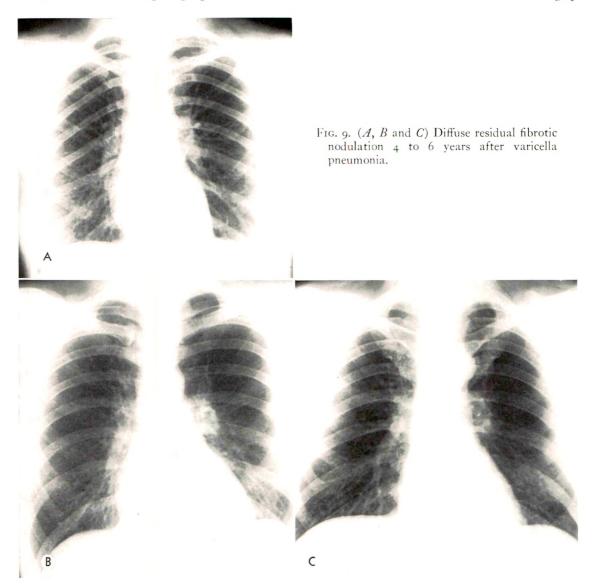
In children, although serious complica-

tions may occasionally occur, pneumonia is usually due to secondary infections with Staphylococcus aureus or Streptococcus hemolyticus, rather than to the varicella virus itself. Exceptions to this are the specific varicella pneumonia encephalitis and nephritis which are occasionally encountered and which may prove fatal. Waring et al.46 quoting Bullowa and Wishik⁶ state that the complication of pneumonia in chickenpox is approximately 0.8 per cent. Empyema is more common after pneumonia complicating chickenpox (14 per cent) than after pneumonia complicating any other contagious diseases, except for scarlet fever (36 per cent). The causative organism in pneumonia associated with chickenpox was most frequently Streptococcus hemolyticus. However, in Bullowa and Wishik's cases there was apparently no case of a primary varicella virus pneumonia. The 8 deaths described in their report were due to secondary bacterial invaders and not primary varicella pneumonia. Although complications in childhood are infrequent, 2 of the 4 children included here had manifestations of bacterial and viral complications. Viral pneumonia was documented histologically, in addition to hemolytic Staphylococcus aureus septicemia and multiple abscesses. Widespread viral invasion of numerous organs of both children suggests probable decrease in host resistance, heightened organism virulence, or both. The remaining 2 children demonstrated widespread viral organ involvement without secondary bacterial infection.

The relationship of the severity of the rash to the severity of the disease has been studied.³³ Lack of constant correlation of the physical signs and the roentgenographic findings is indicated by absence of rales in 9 patients, in spite of marked abnormality of the pulmonary roentgenograms. The roentgenographic findings, especially the nodulation seen, are, of course, not diagnostic of varicella. However, the association with typical skin lesions offers sufficient evidence to establish a correct diagnosis. Felson¹³ emphasized findings similar to our cases; *i.e.*, the pneumonia in-

volves acinar nodules which coalesce and which are best visualized in the thinner peripheral portions of the widespread alveolar infiltrates. The nodules are considerably larger and show a greater tendency to coalesce than interstitial types of nodules due to other disease. The infiltrates have fluffy margins and are segmental or even lobar in distribution. Sometimes, a butterfly pattern, due to large ill-defined coalescent densities, may be seen. Air bronchograms and alveolograms, due to air within intrapulmonary bronchi or alveoli which are adjacent to the exudate filled alveoli, are again indications of an alveolar type of disease. The appearance of the acute acinar nodulations in chickenpox pneumonia is a change which occurs earlier in the course of the disease than the nodular changes observed in chronic interstitial disease. The miliary appearance of the lesions which have been described by some authors may really be complicated by initial edema, stipplings and heavy markings. However, the nodules never assume the clear-cut, discrete independent nodulation of miliary tuberculosis, even after the obscuring factors of edema and stipplings have regressed or disappeared. The anatomic substrate of the stipplings is probably an additional exudate in some of the alveoli. It is capable of condensation by the inspired air and even formation of a localized eosinophilic membrane. These changes are common, but not limited to viral pneumonias.20 Even as long as 9 weeks after clinical recovery, there has been described a fine mesh of interstitial thickening as a visual residuum.²⁵

Among the many conditions which produce acute diffuse miliary or nodular conditions roentgenographically, 13,14 chickenpox pneumonia occupies a characteristic place. Other acute pneumonias of any unusual etiology, such as pneumonias caused by Pneumocystis Carinii, eosinophilic pneumonia of allergic or parasitic etiology, measles and other viruses, salmonella, shigella and leptospira may also cause disseminated alveolar patterns. Pulmonary hemosiderosis, Goodpasture's syndrome, hair-spray pneumonias, mineral oil aspira-



tion, pulmonary edema, pulmonary contusion and even newborn aspiration syndromes and hyaline membrane disease are to be considered as a small number of the many conditions in differential diagnosis.

Roentgenographic improvement lags behind the clinical recovery which generally takes from 1 to 2 weeks. Chemotherapy does not seem to affect the rate of regression of the roentgenographic changes. The slow regression of the pulmonary changes in chickenpox pneumonia, extending over a period of $2\frac{1}{2}$ months, suggests classification of the disease, in some cases, as a subacute or even a chronic miliary process. ¹⁴ Abra-

hams and his co-workers¹ and Knyvett²⁴ describe some chickenpox pneumonias as also possibly falling into a chronic category. They state that varicella pneumonias are a cause of subsequent pulmonary calcifications and emphasize that this must be differentiated from tuberculosis and histoplasmosis as one of the common causes of multiple nodular pulmonary calcifications. In a noncalcified chronic or subacute infection with chickenpox, diseases such as sarcoidosis, miliary tuberculosis, histoplasmosis and carcinomatosis, also have to be excluded.

Follow-up roentgenograms on 9 of our

cases, taken as long as 6 years after the initial infection of the disease, have failed to reveal any evidence of calcifications. However, 6 of the 9 showed definite residual diffuse, fine fibrotic nodules and "beadings" in the lower lung fields which could be ascribed to a varicella etiology (Fig. 9, A, B and C).

Secondary pulmonary invasion by pathogenic bacteria in patients who have chickenpox but who do not have chickenpox pneumonia can cause bronchopneumonias which roentgenographically may resemble varicella pneumonia. However, the true bacterial bronchopneumonia shows a more patchy distribution, coarse hilar bronchial infiltration and lobar or segmental consolidation. This is in contrast to the miliary distribution of a suspected varicella pneumonia. In addition, clinically, bacterial pneumonias will show a leukocytosis with a shift to the left and blood and sputum cultures may reveal the causative organism. Bacterial pneumonias usually appear later in the course of the disease than do varicella pneumonias. 40 This is especially true in the pediatric age group. Of course, it is possible to have a primary varicella pneumonia complicated by a secondary bacterial pneumonia. The specific findings are inclusion bodies in the sputum complicated by bacteria as secondary invaders making both the clinical and roentgenographic diagnosis more difficult.

In true varicella pneumonias, unusual complicating roentgenographic findings may be blunting of the costophrenic angles associated with nonbacterial pleural effusion. Transient, mild cardiac enlargement has been reported early in the disease. 18,46 Other complications include pulmonary edema, mediastinal emphysema and subcutaneous emphysema (most probably from air in the mediastinum). 21

SUMMARY

Although there are a vast number of etiologies capable of producing disseminated lesions in the lungs, it should be possible to recognize at least an alveolar acinar pattern of distribution of the pulmonary

infiltrate. This, with a history of exposure to chickenpox, makes the roentgenographic diagnosis of varicella pneumonia possible in the majority of cases. The presence of diffuse scattered fine residual pulmonary nodulations in 6 of the cases examined as long as 6 years after the infection suggests either residual scarring from acute pleural pox or a chronic varicella etiology in some cases. Postmortem correlation reveals that the cutaneous varicella lesion is matched by similar lesions regularly found in the lungs and pleura as well as the peritoneum and the liver.

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PNEUMOCYSTIS CARINII PNEUMONIA (PLASMA CELL PNEUMONIA)*

ROENTGENOGRAPHIC, PATHOLOGIC AND CLINICAL CORRELATION

By SYDNEY F. THOMAS,† WERNER DUTZ,‡ and ETHYLYN JENNINGS KHODADAD§

THE disease caused by Pneumocystis Carinii is an epidemic parasitic infection presenting with diarrhea and abdominal distention, followed by a malabsorption syndrome. This is accompanied by pulmonary infiltrations of interstitial type, which may be progressive and fatal; especially in the premature, very young, or debilitated patient.

Reviews in recent publications by Post et al.,5 Khodadad et al.,3 and Kohout et al.4 describe some of the material covered in this paper from the physical, medical, epidemiologic and hematologic aspects and form the background for the present communication. Three recent reviews of cases and epidemics in the North American literature cover adequately the past litera-

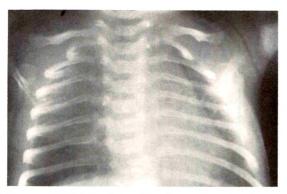


Fig. 1. Child K had a positive bronchial aspirate for Pneumocystis Carinii during the acute phase of the disease. The child improved under PAS-INH therapy, but shortly after therapy was discontinued the child died. At 3 months of age, irregular but confluent infiltrate with more disease proximally was seen. The infiltrate in the parahilar peribronchial region produces an air-bronchogram. Note the thymic silhouette.

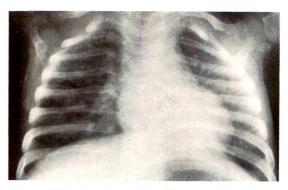


Fig. 2. Fifty-four days after Figure 1, the disease process is more widely spread with more uniform distribution, giving the appearance of an improperly focused reproduction. The roentgenogram was made in partial expiration and this enhances the findings.

ture on roentgenographic findings^{1,2,6} and bring the salient points of the past roentgenographic experiences into focus.

ROENTGENOGRAPHIC OBSERVATIONS

In reviewing the cited papers^{1,2,6} and a textbook, it was noted that the authors tend to oversimplify the findings in an attempt to present a single diagnostic picture which could be recognized easily. This clouds the true pathologic correlation of the changing shadows as observed on serial roentgenograms.

The roentgenograms of the cases in this study demonstrate the dynamic aspect of the shadows from the early to the late phases (15 months) in the disease, with good correlation with the pathologic material (Fig. 1 through 4). No previous roentgenologic-pathological correlations showing whole lung sections of children who

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died shortly before or shortly after the last roentgenogram was obtained have been published (Fig. 5 through 8).

MATERIAL

One hundred and seventeen roentgenograms of 40 cases were reviewed in which clinical data combined with pathologic and laboratory evidence of Pneumocystis Carinii infestation were available and follow-up for a prolonged period was possible. Roentgenograms just prior to or just after death in 14 children were compared with whole lung sections of Pneumocystis infected lungs (Fig. 5 through 8). The findings of 38 autopsy studies were also correlated and sporadic roentgenograms of another 22 clinically suspected cases were studied, bringing the total cases observed to 100, in which a total of 215 roentgenographic observations were made.

METHOD OF FILM REVIEW DURING THE SURVEY

All the roentgenograms of the survey group of 40 children with complete laboratory and clinical data were reviewed without knowledge of the degree of the actual clinical or pathologic manifestations of the disease; *i.e.*, whether or not the patient had been proven to have the disease at all. No details of therapy were known to the re-

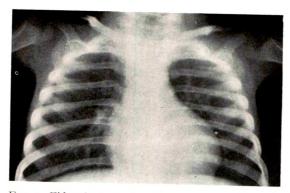


Fig. 3. Fifty-six days after Figure 2, or a total of 110 days after the first examination. The areas of infiltration are sharper in outline in the proximal parahilar region with a slight, almost normal, air-bronchogram being discernible. This roentgenogram was also made during slight expiration.

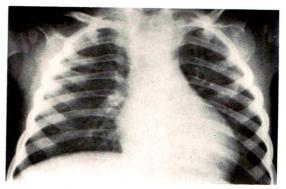


Fig. 4. One hundred and sixteen days after Figure 2, or a total of 226 days after the first examination. Parahilar infiltrates are still sharper but approximately the same in extent. The periphery is now clear. At autopsy, no parasites could be found in the lung sections, while focal perihilar and peribronchial fibroblastic infiltration was still remarkable. The cause of death was respiratory insufficiency.

viewer. The roentgenograms were graded on an "o" to "4 plus" basis for the extent of the disease found. After review of the roentgenograms was completed, the clinical, laboratory and pathologic findings were recorded on a chart with the roentgenologic findings, and correlation or noncorrelation was estimated.

RESULTS

There is no single finding or characteristic infiltrate resulting from this disease which is roentgenographically diagnostic. Although there is no specificity of the pattern of this disease, the roentgenogram of the chest is useful for diagnostic corroboration and in following the course of the disease as manifested in the lungs, either treated or untreated.

Over a period of 15 months, the early roentgenograms are most likely to show a confluent uniform density (glassy), which becomes more irregular in appearance as time passes (Fig. 1 through 4). This early diffuse shadow correlates well with the generalized plasmocellular infiltration and complete consolidation of the lung, in which the parasites fill large numbers of alveoli and bronchioli (Fig. 5; and 6, A, B and C). The shadows seen later are patchier, irregular



Fig. 5. Photograph of a lung specimen. Child S was a female foundling; the admission age was estimated as 3-4 days. She developed diarrhea after 6 weeks. At the age of $2\frac{1}{2}$ months, she developed a respiratory crisis with cyanosis, sternal retraction and diffuse moist rales. Her weight was 2,960 gm. Severe athrepsia was present. Distention of bowel loops was noted through the abdominal wall. Autopsy showed a diffuse consolidation of both lungs, especially in the posterior portion of the right lower lobe. Histologically, there was a very heavy infiltration of the septa with plasma cells. The septa measured 50-60 μ in thickness. Almost all bronchi as well as all alveoli were filled with pneumocyst colonies. The typical picture of acute diffuse pneumocystosis was present in a roentgenogram made at the onset of the respiratory crisis. The child died a few hours after the roentgenogram had been taken. (The roentgenogram was not available for reproduction.)

in distribution and often have an obliquely downward orientation from the hilar region, which gives a streaked appearance to the lungs; yet, the densities are sharper in outline than those seen earlier in the disease (Fig. 7, A and B; and 8, A and B).

Pathologically, one finds only a focal plasmocellular and lymphocytic infiltrate, often arranged around the peribronchial and subpleural areas. This focal lesion may

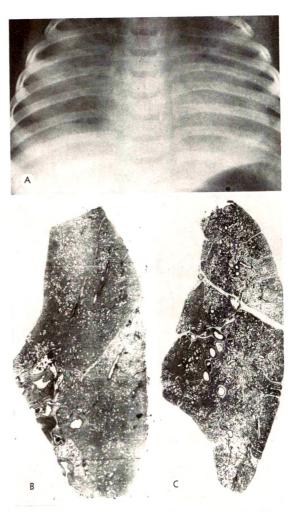


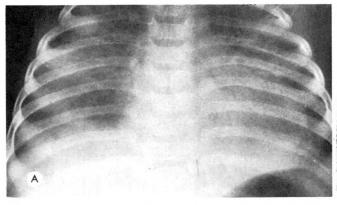
Fig. 6. (A, B and C) Child Sh. was I month old at admission, weighed 3,910 gm. and appeared to be normal. At the age of 2 months, first weight loss was noted. A roentgenogram made at the onset of diarrhea at the age of 3 months, showed focal infiltrations. A second roentgenogram at the age of 4 months, showed more diffuse shadows. A is the third roentgenogram made shortly prior to death at the age of 5 months. The diffuse shadows correlated well with the findings of a severe interstitial infiltration in the septa (B and C). The septa measured between 10 and 50 μ in thickness. Pneumocysts were found scattered throughout the lung although not heavily. This case is representative of a diffuse severe infection which has passed through the plasmocytic into the lymphocytic and macrophagic stage, the heavy shadows being due to the alveolar macrophage obliteration of aeration. Note the distention of the bowel in A, a rather constant finding, also seen at autopsy.

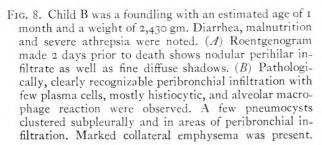




Fig. 7. (A and B) Child R. (A) Lung section showing a confluent infiltrate in the apical portion of the right lung, which produced a uniform apical density in the roentgenogram (B). In the more central portion of the lung, there is an infiltrate with some of the septa widening to 40–50 μ. Histologically, the infiltrate consisted primarily of lymphocytes and histiocytes. Some of the smaller bronchi as

well as some of the alveoli contained macrophages. At the periphery of some of the subpleural alveoli as well as some of the alveoli in the center of the dense infiltrates, a few pneumocysts were found. Note the subpleural infiltrate in the lower lobe, which measured 5 mm. in width. There were also irregular scattered perivascular and peribronchial foci close to the hilus, which would account for the parahilar shadows seen on the roentgenogram. All of the septa were infiltrated with lymphocytes in varying degrees. Mild compensatory emphysema was present. Compare the peripheral hyperaeration on the roentgenogram with the subpleural infiltrate.







never progress in cases of mild infection which do not reach the stage of diffuse infiltration with respiratory crisis and death. It corresponds, however, to a slowly progressing healing process after a more severe infestation with the disease. The peribronchial and subpleural areas retain pneumocysts longer than the other portions of the lungs. The weakened alveolar walls of the healed regions dilate and emphysema is seen side by side with the remaining infiltrates. This latter process is the basis for the change in roentgenographic appearance. In summary, at the height of the disease, this consists of a more or less diffuse shadow which then in the course of the healing process is followed by gradual sharpening of the pulmonary densities, which are irregular in distribution and stand out against a more or less emphysematous background. The infiltrate in the subpleural region remains longer and often measures less than .25 cm. in thickness. This is set off from the surrounding emphysema, producing the paradox of hyperaeration of the periphery of the lung fields (Fig. 8, A and B). In the last stages of the disease, only peribronchial streaking and hyperaeration without special characteristics are found (Fig. 8, A and B).

SUMMARY AND CONCLUSION

- 1. The roentgenographic aspects of pulmonary Pneumocystis Carinii infections correlated well with the pathologic and clinical findings in the over 1∞ cases analyzed in this study.
- 2. Roentgenograms of the chest are useful in the corroborative diagnosis and

prognosis and follow-up of patients with Pneumocystis Carinii infection.

3. Inchildren with unexplained athrepsia, who show interstitial infiltrates on roent-genograms of the chest, Pneumocystis Carinii should be suspected in the face of negative tuberculin tests, or, at least, bronchial washings should be attempted and proper stains employed to detect the organisms of Pneumocystis Carinii.

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PULMONARY COMPLICATIONS FOLLOWING FURNITURE POLISH INGESTION*

A REPORT OF 21 CASES

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HE purpose of this study is to empha-I size the importance of the roentgenographic examination of the chest as a diagnostic procedure in patients accidentally ingesting furniture polish. Ingestion of hydrocarbon products by children under the age of 5 years accounts for a major percentage of poisoning each year, especially where these products are used in the home for cooking, heating and cleaning.2,5 It has been estimated that the incidence of nonfatal cases is approximately 28,000 and the mortality after accidental ingestion of these petroleum distillates accounted for the death of 763 people from 1951 through 1958.6

A review of the literature revealed only 2 reports of large series of cases12,15 in which the clinical features and treatment of patients ingesting furniture polish were discussed. References in the medical literature regarding furniture polish ingestion are less frequent compared to the more commonly ingested kerosene products, 8,18,14,21,22, with very little emphasis being placed on the roentgenologic manifestations of the chemical pneumonitis that so frequently follows as one of the major complications. Toxic effects are more frequent following the ingestion of furniture polish, with more severe pulmonary complications than seen in other cases of hydrocarbon poisoning.6

The pathogenesis of the pulmonary complications is thought to be due to the aspiration of the product directly into the lungs or as the result of absorption from the gastrointestinal tract with subsequent hematogenous transfer to the lungs. Although there is disagreement among those conducting animal experiments, most1,10,15,18,19,23

TABLE I FREQUENCY OF THE VARIOUS HYDROCARBONS INGESTED

Product	No. of Cases	Per Cent	
Kerosene	71		
Furniture polish	21	19.7	
Lighter fluid	6	5.6	
Gasoline	4	3.7	
Turpentine	2	1.9	
Insecticide	2	1.9	
Floor polish	ī	0.9	

feel that aspiration is the most significant mechanism in the pathogenesis of the pulmonary inflammatory changes. Evidence is presented by Deichmann et al.8 to support the thesis that pulmonary injury results primarily from absorption by the gastrointestinal tract with the hydrocarbon being carried to the lung by way of the blood stream and that direct introduction of the hydrocarbon into the lungs by aspiration plays a minor role in the production of the pulmonary inflammatory changes. Recent experimental work by Gerarde¹⁰ and Huxtable et al.16 shows that absorption does occur but it is not of such magnitude as to cause the same degree of changes as seen following aspiration. The ratio of the oral to intratracheal LD₅₀ is approximately 140:1, indicating the significant role of direct contact by aspiration. 10,18

The experimental work by Huxtable et al.,16 designed to compare the physical properties of several commonly used furniture polishes, reveals that the viscosity is low and of the same magnitude as that of kerosene and the hazard of aspiration is considerable. Two physical properties—

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TABLE II

FREQUENCY OF VARIOUS BRANDS OF
FURNITURE POLISH INGESTED

Product*	No. of Cases
Old English furniture polish O'Cedar furniture polish Johnson's Pride Red furniture polish (name unknown)	14 2 1 4 —

^{*} Furniture polish listed by brand names.

low viscosity and low surface tension—increase the aspiration hazard of light hydrocarbons.¹¹ Viscosity determines the likelihood of entry and the rate and extent of penetration into the bronchi, bronchioles, and alveoli in the lungs. The main constituent of Old English and O'Cedar furniture polish is mineral seal oil, a light petroleum oil obtained as a fraction of a distillate from crude petroleum, containing unsaturated and saturated aliphatic and aromatic hydrocarbons.¹⁶

MATERIAL AND COMPLICATIONS

A review of 107 cases of patients who had chest roentgenograms at the Medical College of Virginia Hospital following the ingestion of various hydrocarbon petroleum distillates revealed roentgenologic changes in the lungs in 91 per cent. The ingestion frequency of the various hydrocarbons is listed in Table 1. Furniture polish is usually the second most frequently ingested product.⁶

The following discussion is confined to 21 cases of furniture polish poisoning, with emphasis being placed on the roentgenologic findings most frequently seen in the lungs along with an evaluation of the pertinent and most often encountered clinical and laboratory findings.

The main complications following the ingestion of furniture polish are confined to the lungs and central nervous system. The pulmonary changes include edema, congestion, pneumonitis and, in many instances, necrosis, all of which, if extensive

enough, present the greatest threat to the patient's life and may result in death. These products act as pulmonary irritants when they come in direct contact with the endothelial lining, causing increased permeability, resulting in edema and the passage of fibrin and inflammatory cells into the alveoli with the formation of hyaline membranes, vasothrombi and desquamation of the alveolar lining. The central nervous system changes consist of lethargy, semicoma or coma.

The most commonly ingested furniture polish products are shown in Table 11.

CLINICAL FINDINGS

The average age of the patients was 18 months with the exception of one 23 year old Negro female who attempted suicide by drinking 8 ounces of red furniture polish. Thirteen patients were Negroes and 8 were Caucasians. The sex distribution was about equal. As noted in Table 11, the product was identified by its brand name in all but 4 cases. The amount ingested was known in 13 cases and ranged from 1 teaspoonful to 8 ounces. The initial reaction in 10 patients was that of gagging or strangling, choking or coughing. Nine of these patients had positive roentgen findings on their chest roentgenograms. There were 8 patients who gave no history of the above symptoms, but 7 of this number had positive chest roentgen findings. In 3 patients, no history was available but all had positive roentgen findings. A history of vomiting was obtained in 7 patients, I of this number had vomiting induced by the parents. Six of these patients had positive roentgen findings. In 13 patients a negative response was obtained regarding vomiting, with II having positive roentgen findings. Lethargy was experienced by 14 patients, 13 of whom had positive chest roentgen findings. Seven patients had no evidence of lethargy, with 5 of this group having positive roentgen findings. None of the patients was in a coma nor did any experience seizures. There was an immediate febrile response in all 21 cases, with the average temperature being 103° F. within the first 12 hours. The maximum temperature recorded in the majority of cases was 105° F. with the temperature returning to normal usually within 7 days. There was an increase in the white blood cell count in 12 patients with 3 patients having a normal count. In 6 patients, treated as out-patients, no white blood cell count was obtained. In the majority of those patients having an increase in the white blood cell count, there was also an increase in the polymorphonuclear leukocytes. On admission, 11 patients had positive clinical chest findings on auscultation with all of these showing positive roentgen findings on their chest roentgenograms. Ten patients were found to have clear lungs on admission, with 7 of this number having positive roentgen findings. Of the 18 patients who had roentgenographic evidence of pulmonary inflammatory disease, only 61 per cent had some degree of abnormal physical findings in the lungs on auscultation. There were 16 patients hospitalized (77 per cent) with the average stay in the hospital being 7.6 days, ranging from I to 24 days. An analysis of the patients ingesting kerosene and other hydrocarbons listed in Table 1 reveals that only 62 per cent of the patients were hospitalized, with the average stay in the hospital being 4.4 days. Gastric lavage was performed in 6 patients, with all but I failing to show positive find-

Table III
PULMONARY COMPLICATIONS BY PRODUCT INGESTED
AND DEGREE OF INVOLVEMENT

Product	No. of Cases	Positive Roentgeno- grams	Degree of Involve- ment
Furniture polish	21	86%	minimal 38% mild 28% moderate 12% severe 22%
Kerosene and other hydrocarbons	86	92%	minimal 41% mild 42% moderage 17% severe 0%

Table IV

DISTRIBUTION OF THE PULMONARY INFLAMMATORY
CHANGES FOLLOWING INGESTION OF FURNITURE
POLISH IN PATIENTS WITH POSITIVE

ROENTGENOGRAMS

Involvement	No. of Cases
Both lower lobes	14
Both lower lobes and right middle lob	e
consolidation	I
All lobes involved with right middle lob	e
consolidation	3
Total	18

ings. There were 15 patients who had chest roentgenograms within the first 5 hours following ingestion of the furniture polish, with all of this number having positive roentgen findings. The remaining 6 patients of this series had chest roentgenograms taken after 12 hours following ingestion, with all showing positive roentgen changes.

There were 2 reported deaths in this series, one resulting from the ingestion of Old English furniture polish and the other from O'Cedar furniture polish. One death occurred in the group ingesting kerosene and other hydrocarbons listed in Table 1. This patient showed only mild roentgen changes in the lungs.

ROENTGEN FINDINGS

Roentgenologic changes in the lungs were found in 86 per cent of the 21 cases of those patients ingesting furniture polish. Eightysix or 92 per cent of patients ingesting kerosene and other hydrocarbons showed roentgen changes. The severity of involvement is listed in Table III and shows that the degree of involvement was more marked in the group ingesting furniture polish (22 per cent for the furniture polish group vs. 0 per cent for the group ingesting kerosene and other hydrocarbons).

The most dependent portions of both lungs were most frequently involved with mottled densities distributed primarily in the lower lobes and perihilar areas. As the

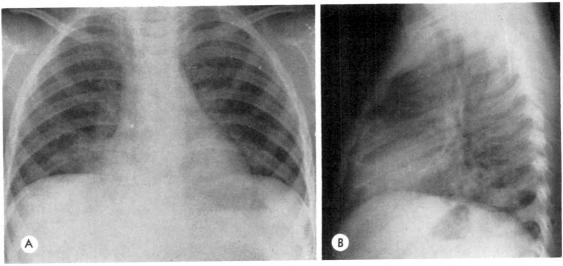


Fig. 1. Case 1. Chest roentgenograms taken 7 hours after ingestion of furniture polish. (A) Frontal roentgenogram shows mild mottled densities adjacent to both lower heart borders. (B) Lateral roentgenogram shows the densities in the lower lobe and perihilar areas.

pulmonary inflammatory changes progressed, there was some evidence of confluence of the densities with areas of consolidation becoming apparent in the right middle lobe in many instances. The distribution of the lesions in 18 cases is shown in Table IV.

In none of the 18 cases with positive roentgen findings was there any evidence of pleural effusion, pneumomediastinum pneumothorax or other changes described in the literature^{3,17,20} as frequently complicating hydrocarbon pneumonitis.

REPORT OF CASES

CASE I. An 18 month old Negro male drank a mouthful of red furniture polish. There was a history of choking and coughing but no vomiting following ingestion of the polish. The patient was brought to the Pediatric Out-Patient Clinic approximately 6 hours following ingestion of the toxic material and a chest roentgenogram was obtained I hour later. On physical examination the temperature was 103.5° F., pulse 110 per minute and respiration 35 per minute. There was a mild degree of lethargy and scattered rhonchi were heard in both lungs on auscultation. The patient was treated with antibiotics and aspirin and followed as an out-patient. The chest roentgenogram, showed mild mottled densities in both lower lobes (Fig. 1, A and B). On the following day the temperature was 101.3° F., and on auscultation the chest was clear. Recovery was complete and uneventful. There were no residual changes on follow-up chest roentgenograms.

CASE II. A 30 month old Negro male drank one tablespoon of Old English furniture polish approximately 20 minutes before being brought to the Emergency Room. There was a history of coughing and gagging, but no vomiting. On physical examination the temperature was 100.2 F., and the lungs were clear on auscultation. A chest roentgenogram taken I hour following ingestion of the polish (Fig. 2A) showed mild mottled densities adjacent to the lower cardiac border with the pulmonary inflammatory changes confined to the lower lobes and perihilar areas. The patient was treated with antibiotics with no gastric lavage performed at that time. He was discharged to be treated as an out-patient, but was returned to the hospital on the following day because of an elevation in temperature and an increase in the rate of respiration. Physical examination on admission revealed a moderately lethargic child with a temperature of 103.4° F., pulse 160 per minute and respirations 60 per minute. There were bilateral rhonchi heard with inspiratory intercostal retractions seen in the chest. The remaining physical examination was not remarkable. The white blood cell count on admission was 15,000 which on the third hospital day rose to 18,500.

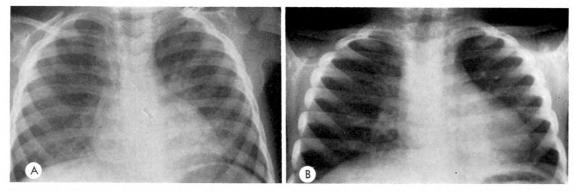


Fig. 2. Case II. (A) April 23, 1962: Chest roentgenogram taken I hour after ingestion of furniture polish showing mild mottled densities adjacent to both lower heart borders. (B) June 15, 1962: Frontal roentgenogram showing clearing of pneumonitis after nearly 8 weeks.

On the second hospital day the temperature reached 105.0° F., but returned to normal in 4 days. The patient was treated with antibiotics and oxygen mist in a croupette. Follow-up chest roentgenograms showed very little change from the initial roentgenogram. Clinically, the patient improved rapidly and was discharged on the eighth hospital day. A chest roentgenogram approximately 8 weeks later (Fig. 2B) showed complete clearing.

Case III. A 16 month old Negro male drank an unknown amount of Old English furniture polish 4 days prior to his admission to the hospital. Immediately after this, the patient was seen by the referring physician who did a gastric lavage and treated him with antibiotics. On the following day the patient's temperature was 103.0° F., with an increase in the respiratory rate and mild lethargy. On admission to the hospital, he was in moderate respiratory distress with a temperature of 103.6° F., pulse 160 per minute and respirations 80 per minute. There were rhonchi and rales in both lung fields on auscultation, with dullness to percussion in both lung bases. Chest roentgenograms on admission to the hospital (Fig. 4, A and B) showed severe involvement bilaterally with some beginning confluence of the mottled densities in both lungs. Treatment consisted of antibiotics and oxygen mist in a croupette. The temperature remained elevated for the next 3 days and then gradually subsided to normal. On admission, the white blood cell count was 7,800 and reached 18,500 on the fourth hospital day. Chest roentgenograms 4 and 11 days following admission the pneumonitis. The patient was discharged Amore alert, but the temperature was 104.0° F.

on the 14th hospital day, markedly improved clinically, although there was still roentgen evidence of pulmonary inflammatory changes.

Case IV. A 23 month old Negro female drank less than 3 ounces of Old English furniture polish I hour and I5 minutes prior to her admission to the Emergency Room. The parents gave no history of the child coughing, strangling or vomiting. The patient appeared alert, with no evidence of any respiratory distress. The chest was clear to auscultation. Gastric lavage was not done. A chest roentgenogram obtained approximately 3 hours following ingestion of the polish (Fig. 4A) showed bilateral mottled densities in both lower lobes and perihilar areas of moderate degree, with some beginning right middle lobe consolidation. The patient was admitted to the hospital and treated with antibiotics and oxygen mist in a croupette. Approximately 18 hours following ingestion of the polish, she became moderately lethargic, with some respiratory distress manifested by grunting, wheezing and moderate intercostal retraction. At that time the temperature was 101.8° F., pulse 130 per minute, and respirations 40 per minute. Clinical examination of the chest revealed rhonchi and wheezes in both lungs with only a few rales in the lung bases. A second chest roentgenographic examination (Fig. 4, B and C) on the second hospital day showed further progression of the pulmonary inflammatory changes bilaterally, with involvement of all the lobes to some degree. The white blood cell count was 34,800 with 90 per cent polymorphonuclears on the second hospital day. On the third (Fig. 3, C and D) showed progressive clearing of hospital day, the patient seemed somewhat

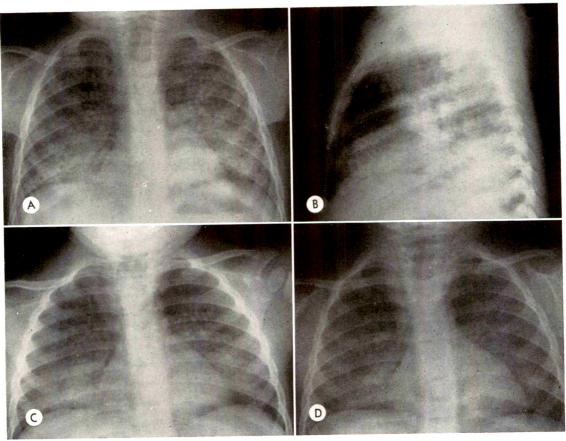


Fig. 3. Case III. (A) April 23, 1964: Frontal roentgenogram 4 days following ingestion of furniture polish showing severe involvement of the lower lobes primarily, with mottled densities in the upper lobes also. (B) April 23, 1964: Lateral roentgenogram showing areas of consolidation in lower lobes and perihilar areas. (C) April 27, 1964: Frontal roentgenogram 4 days later showing considerable resolution of the pneumonitis. (D) May 4, 1964: Further clearing seen on frontal roentgenogram 7 days later with some residual densities remaining in the lower lobes.

and a chest roentgenogram (Fig. 4D) showed further involvement of all lobes. The patient's clinical course became progressively worse and she died on the fourth hospital day.

An autopsy was performed by the Office of the Medical Examiner and the following pertinent pathologic findings were noted. Both lungs were very firm (Fig. 5, A and B) with a combined weight of 365 gm. (normal weight of lungs for a child this age is 155–165 gm.). The pleural surfaces of all lobes were slightly nodular with some evidence of subpleural atelectasis. The cut surface of one lobe showed a marked degree of consolidation, with globules of oil present on the cut surface. There was congestion of the liver, spleen and kidneys. The brain and spinal cord were not examined. Microscopic examination of sections of all lobes of both lungs revealed

extensive bronchopneumonia. The alveolar spaces were filled with fibrin, coagulated protein and cellular debris (Fig. 5, C and D). Most of the alveoli were lined with a fibrin membrane with some desquamation of the walls of the alveoli. Frozen sections of formalin fixed tissue stained with oil red o stain revealed small globules of material in the alveoli and also within many of the macrophages. There was evidence of hyperemia and interstitial edema of the peribronchial tissues. Very few areas of emphysema of the lung parenchyma were noted on any of the sections. The cause of death was attributed to extensive chemical pneumonitis following the ingestion of furniture polish.

Although there was no history of strangling or vomiting in this patient which would leave one to believe that there was no aspiration into the tracheobronchial tree, there was prompt appearance of pulmonary inflammatory changes on the initial chest roentgenograms made within 3 hours following ingestion of the toxic material. Very frequently, the parents are not present when the child ingests the polish and have very little idea of how much was ingested or if the child did, in fact, choke, cough or gag.

DISCUSSION

Roentgenographically, there were several significant findings, some of which have been emphasized by others in the literature. The high incidence of positive roentgen findings in those patients having chest roentgenograms has been noted by many. 4, 7,9,12,14 In this series, it was found to be 86 per cent in those ingesting furniture polish and 92 per cent in the group ingesting kerosene and other hydrocarbons. The early appearance of pulmonary inflam-

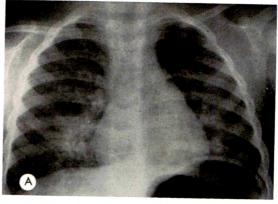
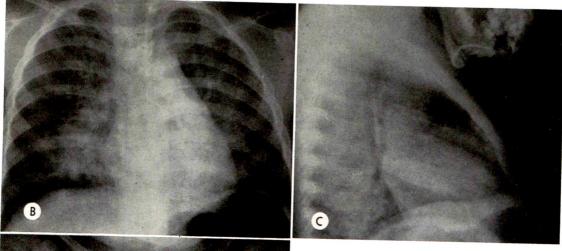


FIG. 4. Case IV. (A) March 3, 1965: Frontal roent-genogram taken on day of admission showing bilateral mottled densities adjacent to both cardiac borders with some early consolidation in the right lower lobe.

matory changes on chest roentgenograms is noteworthy, the changes appearing within 30 minutes following ingestion of the toxic



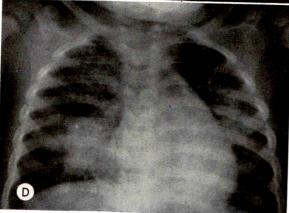


Fig. 4. (B) March 4, 1965: Frontal roentgenogram taken on second hospital day shows more extensive involvement of all lobes of both lungs. (C) March 4, 1965: Lateral roentgenogram shows the wide distribution of the densities with consolidation in the right middle lobe. (D) March 5, 1965: Frontal roentgenogram taken on third hospital day and I day prior to death shows more consolidation in the right middle lobe with somewhat more involvement of the other lobes also.

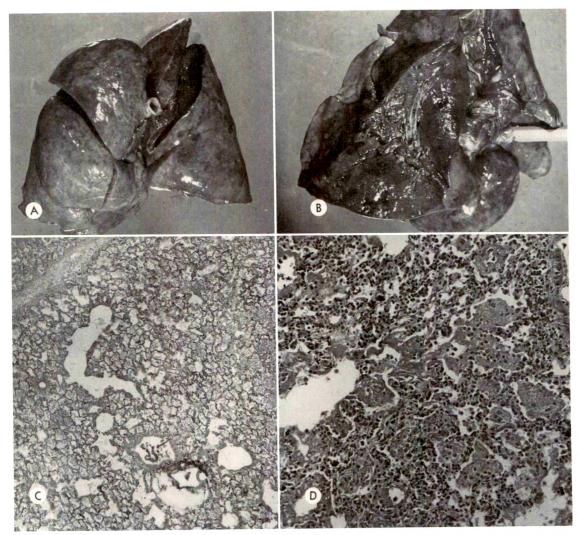


Fig. 5. Case IV. (A and B) Gross specimens of lungs. Combined weight of both lungs was 365 gm., with the pleural surface having a nodular appearance. Cut surface of one of the lobes showing the "liver-like" appearance of the lung parenchyma which was quite firm, with all lobes appearing consolidated. Oily globules were scraped from the cut surface of the lung. (C) Photomicrograph of lung parenchyma showing the marked degree of consolidation in the alveoli (×35). (D) Photomicrograph of lung parenchyma showing diffuse involvement with the alveolar spaces filled with fibrin, coagulated protein and cellular debris consisting of polymorphonuclear lymphocytes and desquamated lining cells. Some of the alveoli show a hyaline membrane (×40).

material in many cases. This would strongly suggest that aspiration does play the major role in the production of the pneumonitis seen in many of the cases. Daeschner *et al.*⁷ showed quite well in their series the influence of time upon the appearance of positive roentgen findings on the chest roentgenogram, with 98 per cent of those who had chest roentgenograms

showing some degree of pneumonitis within the first 12 hours. In this small series of furniture polish poisoning cases, 86 per cent of those with positive chest roentgenograms showed changes within the first 12 hours. There was more extensive involvement in the furniture polish group (Table III) as compared with the group ingesting kerosene and other hydrocarbons. The reason

for this is not clear but some have attributed it to the amount ingested¹² or to the toxic material found in furniture polish.^{12,16}

The distribution of the densities varied only with the severity of the amount of lung parenchyma involved. The majority of cases showed changes in the lower lobes and perihilar areas, with involvement of all the lobes in the more severe cases. The picture differs very little from that in any type of aspiration pneumonitis or bronchopneumonia on the basis of infection. A truer picture of the frequency and degree of involvement could be obtained if a chest roentgenogram were obtained immediately following ingestion of the toxic material, with follow-up studies obtained within the next 12 and 24 hours.

There was no significant correlation of coughing, choking, vomiting or lethargy with the frequency of positive roentgen findings, with changes occurring about equally in those who did and those who did not experience any of these signs or symptoms. Of the 18 patients with positive roentgen findings, 61 per cent had positive clinical findings on examination of the chest, which is a larger percentage than that recorded in the literature. 4,7,9,12,14 This fact is most likely the result of selecting only those patients who had chest roentgenograms on admission. The clinical findings varied considerably on auscultation of the chest, with several patients having a clear chest and rather extensive involvement on the chest roentgenogram. Quite often many of these patients are seen with superimposed upper respiratory infection which makes it difficult to determine the severity of the pulmonary inflammatory changes. The chest roentgenogram remains the best means of evaluating the lungs with most investigators, 4,7,9,14 indicating an unusually high incidence of positive changes on the initial roentgenogram or on subsequent roentgenograms within the first 12 hours. Chest roentgenography of all patients with a history of ingesting any type of hydrocarbon would help considerably in the management of these patients.

The presence of lethargy in many of the patients on the initial examination would indicate that absorption does take place in the gastrointestinal tract and, to a degree, enough to cause central nervous system depression but not in amounts large enough to cause pulmonary complications. 10,16 In this series, I patient, a 23 year old Negro female, drank 8 ounces of red furniture polish, attempting suicide, and was seen approximately 2 hours following ingestion of the toxic material. She denied choking, strangling or vomiting and gastric lavage was done with no aspiration taking place during the procedure. She experienced only very mild lethargy. Chest roentgenograms 3 and 24 hours later were negative. Many¹, 10,11,16 feel that in order for an excretory type of pneumonitis to take place a very large quantity of the polish must be ingested and absorbed in the gastrointestinal tract and, subsequently, be excreted by the lungs, causing a wide distribution of the inflammatory changes in the lung parenchyma.

The treatment of these patients resulted in the uneventful recovery of all but 2, who died as the result of extensive pulmonary complications. All were given antibiotics and in those experiencing respiratory difficulty oxygen mist was used. The role played by gastric lavage in these patients was not conclusive, with roentgen changes occurring about equally in those who were lavaged and those who were not lavaged. A cooperative study of the ingestion of kerosene and other petroleum distillate products showed that gastric lavage was not harmful to the patients, but there was no conclusive evidence that it was beneficial. Most agree that gastric lavage should not be done unless an unusually large amount has been ingested, because of the added risk of causing aspiration of the gastric contents into the lungs. 6,7,10,12 Recent investigations^{1,10} on the use of mineral oil, olive oil, and fats and their effect on absorption of hydrocarbons from the gastrointestinal tract are inconclusive and require further study. Again, the introduction of these substances into a young child may be quite hazardous and possibly may lead to a lipoid pneumonia.

The use of aerosol furniture polishes could perhaps reduce the morbidity and mortality considerably, since it is highly unlikely that a child could spray enough polish directly into his mouth to create an aspiration hazard such as would exist with a hydrocarbon in the liquid form.¹¹

SUMMARY AND CONCLUSION

A study of 21 cases of furniture polish poisoning has been made, with emphasis on the roentgenographic features of the disease and other pertinent clinical findings. A comparison was made between a group ingesting furniture polish (21 cases) and those ingesting kerosene and other hydrocarbons (86 cases) regarding roentgenographic evidence of pulmonary complications, with no appreciable difference being noted in the frequency of the changes. There was found, however, a difference in the severity of the pulmonary inflammatory changes seen on the chest roentgenogram, with the furniture polish group showing the more severe involvement. In the majority of cases, chest roentgen findings were found to be present within the first 12 hours following ingestion of the toxic material in both groups. The group ingesting furniture polish was hospitalized more frequently and for a longer period of time and manifested a more severe clinical course. There was no significant correlation between the positive chest roentgen findings and the frequency of strangling, vomiting, or the performance of gastric lavage in the smaller group ingesting furniture polish. The routine use of chest roentgenography in all cases of accidental ingestion of hydrocarbon petroleum distillates appears to be quite worthwhile, since clinical evaluation of the chest is less than satisfactory in most instances and not an accurate method of determining the extent of pulmonary complications. The use of aerosol type furniture polishes could perhaps help reduce the

morbidity and mortality in children in this ever present hazard.

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THE LUNGS AND PLEURA IN RHEUMATOID ARTHRITIS*

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RHEUMATOID arthritis, despite its name, is by no means a disease of the joints alone. Over the past few years it has become apparent that visceral involvement in this disease is not uncommon and, when present, it is often accompanied by characteristic roentgenographic findings. Although it has been known for many years that rheumatoid arthritis is a systemic affliction, it was not until 1948 that Ellman and Ball⁸ called attention to the pulmonary manifestations of the disease. Since then there has been increasing interest in "rheumatoid lung disease" and as our awareness of this entity increased, so did the frequency with which we recognized the lung lesions. Over the past 6 years we have encountered a fair-sized group of patients with rheumatoid arthritis who have had nearly every known type of pulmonary involvement, and it is felt that the clinical and roentgenologic findings in these subjects are of sufficient interest and diversity to merit being included in a short review article. Unfortunately, we are unable to determine what proportion of the total number of patients seen at this hospital with rheumatoid arthritis has had pulmonary lesions. It is stressed that this review is not intended to be exhaustive for we believe, along with Burke, that exhaustive reviews exhaust the reader.

Rheumatoid arthritis may affect the lung in several ways. These may be conveniently divided into five groups.

I. NONSPECIFIC CHANGES: PLEURITIS, PNEUMONITIS, BRONCHIECTASIS AND BRONCHITIS

We have frequently seen subjects with rheumatoid arthritis who show roentgenologic evidence of old pleurisy and there seems to be little doubt that this sort of pleural reaction is met with more commonly in subjects with rheumatoid arthritis than it is in a comparable control group.22 Frank pleural effusion is less frequent, and when encountered, it is often difficult to show a cause and effect relationship between the rheumatoid arthritis and the effusion. Nevertheless, in rare instances careful studies have clearly established that an effusion may be an integral part of the rheumatoid process.9 With the widespread use of needle biopsy of the pleura, it is reasonable to assume that histologic confirmation of rheumatoid pleuritis will become increasingly frequent.

We have also seen subjects who have developed areas of pneumonitis at some time in the course of their disease. The roentgenologic and clinical features of this type of parenchymal disease are protean, and, in general, resolve either spontaneously or in spite of treatment. It is unlikely that these nonspecific infiltrates have a common origin, and while some are undoubtedly the result of viral or bacterial infections, others have many of the features of an aspiration pneumonia.

We have encountered one patient with severe deforming arthritis and bronchiectasis. The symptoms of the latter disease, which in this instance were cough, sputum and rarely a minor degree of blood tingeing of her sputum, developed some considerable time after the onset of her rheumatoid arthritis. Nonetheless, the anatomic changes in her bronchi may well have been present since childhood for the bronchiectasis became symptomatic shortly after she was put on steroids. Her left lower lobe

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was resected at another hospital against our advice. No specific rheumatoid changes in the resected specimen were reported from the other institution, but, unfortunately, it did not prove possible for our pathology department to examine adequately the whole lobe.

There seems little doubt that the incidence of these nonspecific pleural and parenchymal lesions has increased since the advent of steroids. Studies have clearly demonstrated that steroid therapy increases the likelihood of subjects with rheumatoid arthritis developing this type of pulmonary complication.²²

2. DIFFUSE INTERSTITIAL PNEUMONITIS AND FIBROSIS

While it is generally accepted that rheumatoid arthritis may be seen in association with diffuse interstitial fibrosis, there are some who doubt that the pulmonary changes are a specific manifestation of the rheumatoid process.²² Histologic examination of the lung in these subjects shows an interstitial fibrosis of nonspecific character with thickened septa and distorted alveolar spaces. Initially, the changes may be those of a pneumonitis with little fibrosis but, as time progresses, more and more fibrosis develops.^{7,19} Exceptionally, the process

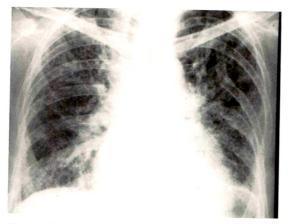


Fig. 1. Standard posteroanterior chest roentgenogram showing diffuse interstitial fibrosis. Although this 43 year old female had no overt evidence of rheumatoid arthritis, she did have early morning stiffness and a strongly positive latex fixation test.



Fig. 2. Close-up view of the right lung field shown in Figure 1.

begins with localized involvement of certain regions of the lung and, more rarely still, burns itself out leaving regional stigmata only. The microscopic appearances of the type of diffuse interstitial fibrosis found in rheumatoid arthritis cannot be distinguished from the idiopathic variety.

Clinically, patients with interstitial fibrosis present with shortness of breath and a dry cough. The physical signs are almost pathognomonic: the subject is usually markedly tachypneic at rest with a respiratory rate of around 30 to 40 in the complete absence of dyspnea, clubbing is frequent as is cyanosis, and coarse rales are heard all over the chest. Pulmonary function studies are characteristic of a diffusion fibrosis with decreased lung volumes, a reduced arterial pO2 which often but not always drops further with exercise, a low or normal arterial pCO2 and a reduced compliance. If the chest roentgenogram suggests the presence of a diffuse interstitial process, it is felt that the diagnosis can be made with reasonable certainty even in the absence of a lung biopsy. The typical roentgenographic fea-

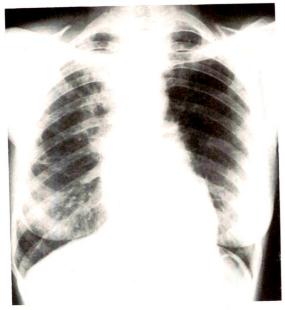


Fig. 3. Case I. Standard posteroanterior chest roentgenogram of a 35 year old Negro female with rheumatoid arthritis and burnt out interstitial fibrosis limited to the upper and mid zones. A patchy pneumonic process is present in the right upper lobe.

tures are shown in Figures 1 and 2. The patient shown in these figures had histologic confirmation of her disease and a strongly positive latex fixation test. She does not at present have any overt evidence of rheumatoid arthritis, although she does have some early morning stiffness.

When rheumatoid arthritis is found in conjunction with the above clinical features, it seems reasonable to assume that the lung disease is part and parcel of the rheumatoid diathesis. Yet, statistical evidence to confirm this impression is most difficult to obtain as the association between diffuse interstitial fibrosis and rheumatoid arthritis is so uncommon.16 Notwithstanding the lack of positive statistical proof for this association, further circumstantial evidence is available which points to the interstitial pulmonary process being rheumatoid in origin. First, there have been several case reports in which anarthritic subjects have been described who presented with diffuse interstitial fibrosis and who also had rheumatoid factor present in their

serum. Some have subsequently gone on to develop rheumatoid arthritis.11 This suggests that pulmonary fibrosis, in association with a positive serologic test for rheumatoid factor, may be either the first manifestation or occasionally the sole manifestation of rheumatoid arthritis.21 Over the past 4 years we have seen 12 subjects with unequivocal chronic diffuse interstitial fibrosis of whom 7 had the diagnosis confirmed by lung biopsy. These subjects would fall into what Scadding20 refers to as "fibrosing alveolitis;" a term that seems to appeal more to its originator than to anyone else. No less than 5 of these had a positive latex fixation test, thereby indicating the presence of rheumatoid factor or factors in their serum. Although it is only a clinical impression, it was felt that these same 5 subjects responded better to steroids than did the others. In some instances, there was an improvement in arterial pO2 and vital capacity following steroid therapy but we are reluctant to claim a cause and effect relationship in view of the small number of subjects. The demonstration of auto-antibodies to lung tissue and the presence of rheumatoid factor in some subjects with a

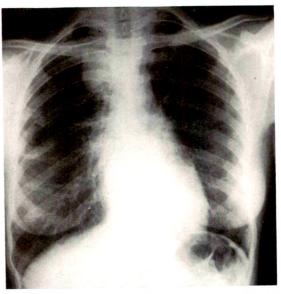


Fig. 4. Case I. Later study showing an infected fluid filled cyst in the right paramediastinal area.

diffusion fibrosis with or without associated rheumatoid arthritis have led some workers to postulate that chronic interstitial fibrosis is an auto-immune disease. This hypothesis remains pure speculation and adds little to the management of patients with this serious lung disorder.

Occasionally, diffuse interstitial fibrosis will burn itself out and the subject will be left with "honeycomb lungs." This is a rare happening but we have seen it on one occasion.

CASE EXAMPLE

Case I. The patient is a 35 year old Negro female who has had rheumatoid arthritis for 15 years. The disease has been inactive for the past 5 years, but she has been left with marked bone deformity and gross restriction of movement in her wrists, ankles and knees. Currently, her plain chest roentgenogram shows a fibrotic process extending throughout both upper zones. Her latex fixation test is now moderately positive but has been strongly positive in the past. In late 1964 she developed a patchy right upper lobe infiltrate which on the plain chest roentgenogram suggested tuberculosis. The latter impression was not confirmed and it became



Fig. 5. Case I. Tomographic cut showing the paramediastinal cyst (arrow) after the fluid has disappeared.

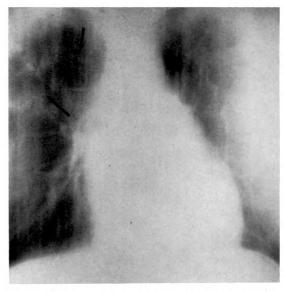


Fig. 6. Case I. Additional tomographic cut showing "honeycombing" elsewhere in the right upper lobe (arrows).

apparent from tomography that she had multiple cysts present in the upper lobes. One of them adjacent to the mediastinum became infected and appeared as a rounded paramediastinal shadow. A mediastinal tumor was strongly considered; however, it was elected to treat her expectantly and the lesion resolved over the next 6 weeks. These appearances are shown in Figures 3 through 6. Presently, she is doing well and her only complaint is occasional morning stiffness and slight productive morning cough.

3. THE NECROBIOTIC PULMONARY NODULE

Very exceptionally, nodules are found in the lungs which are histologically indistinguishable from the typical rheumatoid nodule found on the elbow or tendo-achilles. These nodules must be differentiated from those found in Caplan's syndrome. We have had only I patient under our care with this type of rheumatoid lung.

CASE EXAMPLE

Case II. This subject is a white female, aged 43 years, who developed rheumatoid arthritis II years ago. The disease ran a slow but progressive course, characterized by remissions and exacerbations, until 2 years ago since which time it has been quiescent. At present, she has marked deformity of her hands and feet. Four

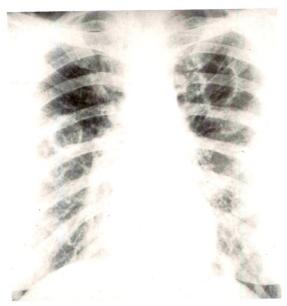


Fig. 7. Case II. Standard posteroanterior roentgenogram (May, 1962) showing cavitated necrobiotic rheumatoid nodules.

years ago, a routine chest roentgenogram demonstrated the presence of multiple rounded nodules in both lungs, some of which were cavitated (Fig. 7 and 8). Because of the abnormal findings, she was admitted to a hospital in Pittsburgh. Detailed investigation revealed no evidence of tuberculosis, fungous infection or malignancy and her tuberculin, histoplasmin

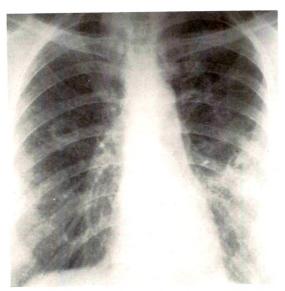


Fig. 8. Case II. Subsequent chest roentgenogram (August, 1965) showing change in size of the nodules.

and other skin tests were negative. She was discharged without a diagnosis. In February, 1965, she was admitted to another Pittsburgh hospital with a left spontaneous pneumothorax. This appeared to have originated from a large subpleural cavitating nodule which had ruptured into the pleural space. The pneumothorax responded to tube drainage and she was allowed to return home. In October, 1965, she was admitted to University Hospital. At the time of admission, she had rheumatoid nodules on her elbows and tendo-achilles. Her latex fixation test was positive to a dilution of 1:5,120. A right lung biopsy was performed, although it was felt reasonably certain that the lesions in her lung were rheumatoid nodules. At operation, multiple nodules were palpable but the intervening lung felt normal. Histologic examination of the resected specimen revealed the typical findings of a rheumatoid nodule (Fig. 9 and 10). The intervening lung tissue was normal on microscopic examination and there was no evidence of pneumoconiosis.

Comment. Pulmonary rheumatoid nodules are said to occur more frequently in men but the absolute number of cases reported is less than 20.15 They are usually multiple, frequently undergo cavitation, and are associated with the presence of

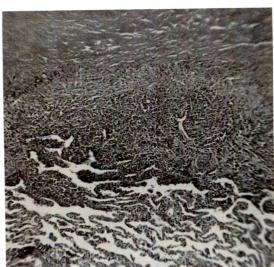


Fig. 9. Case II. Photomicrograph (×100) of a necrobiotic nodule showing necrotic debris in the upper field. Below this can be seen typical palisading and lower still can be seen an area with marked cellular infiltration. At the lowermost edge normal lung is present.

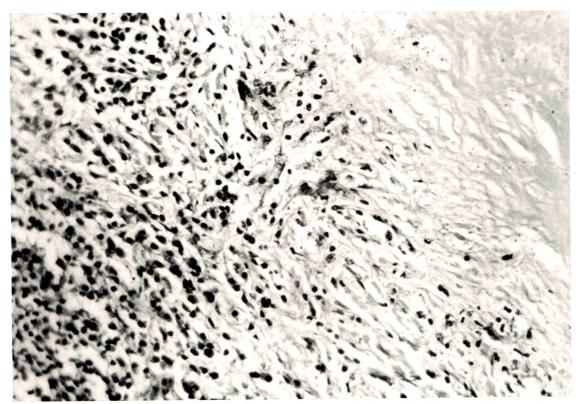


Fig. 10. Photomicrograph (×300) of the same necrobiotic nodule. Higher powered view showing palisading abutting onto the necrotic center.

nodules on the elbow or elsewhere. In our subject there was documented waxing and waning of the size of both the pulmonary and peripheral nodules with the activity of her rheumatoid arthritis. It must be stressed that a diagnosis of this type of pulmonary involvement must be made partly by exclusion, as tuberculosis and fungous diseases are not infrequent complications of rheumatoid arthritis, especially when the latter is being treated with steroids. At times, it is necessary to resort to lung biopsy to confirm the clinical impression, but, in general, the diagnosis can be made without this rather drastic measure.

4. CAPLAN'S SYNDROME

In 1953, Caplan,³ while looking at a series of roentgenograms of coal miners with progressive massive fibrosis, noticed that a minority of them had certain distinctive features. When he visited these subjects, he found to his surprise that over

50 per cent had rheumatoid arthritis. This observation led to further epidemiologic and pathologic studies, and, as a result, it was conclusively demonstrated that a small proportion of subjects with pneumoconiosis did indeed develop parenchymal lung nodules with several characteristic features. 10,12

Caplan's syndrome or rheumatoid pneumoconiosis, although originally described in a coal worker's pneumoconiosis, may be found in almost any subject who has a mineral pneumoconiosis. It has been reported in subjects with asbestosis,23 in classic silicosis,5 in manufacturers of soap abrasives,6 and in a boiler scaler.2 The nodules in the lungs tend to be considerably smaller (1-2 cm.) than the conglomerate lesions of progressive massive fibrosis. They are usually rounder, are fairly well circumscribed and tend to be more peripheral (Fig. 11). Necrosis is frequent and, exceptionally, if the nodule is large, the cavitation may be confused roentgenographically

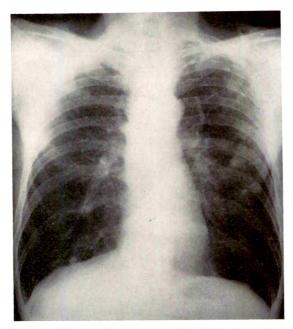


Fig. 11. Standard posteroanterior chest roentgenogram showing typical Caplan nodules. This subject had anarthritic rheumatoid pneumoconiosis as a complication of asbestosis. (Reproduced with permission from *Thorax*.³)

with tuberculosis.¹⁷ Less frequently, the nodules are smaller and diffusely scattered throughout both lung fields, in which case the roentgenographic appearance then resembles simple Category 3 pneumoconiosis.4 Like the necrobiotic nodule, the Caplan nodule may fluctuate considerably in size and often, when the systemic disease goes into remission, the nodule becomes smaller. In approximately 40 per cent of subjects with typical Caplan nodules, systemic rheumatoid arthritis is absent, although some of these subjects later go on to develop the disease. Thus, the appearance of pulmonary nodules may antedate the joint manifestations of the disease by several years. The vast majority of subjects with anarthritic Caplan's syndrome have rheumatoid factor or factors 'present in their serum. In contrast to progressive massive fibrosis, rheumatoid pneumoconiotic nodules may develop rapidly, often in as little as 2 to 3 weeks; and, furthermore, there is a tendency for them to appear in crops. Over the past 6 years, we have seen 4 patients with Caplan's syndrome, 2 of whom have appeared in the literature as case reports.^{13,14}

The rheumatoid pneumoconiotic nodule macroscopically bears a resemblance not only to the large silicotic nodule and the tuberculous nodule, but also to the pulmonary rheumatoid necrobiotic nodule which is found in the absence of pneumoconiosis. Unlike the silicotic nodule, that of Caplan frequently forms clefts and may undergo cavitation and in this way superficially resembles the conglomerate lesion of progressive massive fibrosis. Several Caplan nodules may coalesce and form a larger confluent nodule.10 In many instances, concentric layers of dust laden macrophages can be seen on the periphery of the lesion. Histologically, the center of the nodule contains necrotic debris. Outside the area of necrosis, there may be some palisading but this is far less marked than in the typical necrobiotic nodule. More peripherally still, there is an area of subacute inflammation which has been called the rheumatoid or inflammatory zone by Gough and his co-workers.¹⁰ This region is characterized by marked cellularity and is infiltrated with polymorphonuclears, plasma cells and lymphocytes. The rheumatoid zone is not present in the silicotic nodule nor is it present in progressive massive fibrosis or tuberculosis. Nonetheless, histologic or cultural evidence of tuberculosis is present in around 30 per cent of Caplan nodules.10

The etiology of Caplan's syndrome remains a mystery. It has been suggested that the Caplan nodule is a modified rheumatoid nodule occurring in the lung and that the prior inhalation of dust has damaged the lung in a similar fashion to the manner in which pressure has damaged the subcutaneous tissue over the olecranon processes. It has been further suggested that this prior dust injury predisposes to the development of lung nodules in subjects with the rheumatoid diathesis. This hypothesis, although superficially alluring, does not explain why Caplan's lesions are

most commonly found in the less severe categories of simple pneumoconiosis, i.e., o and I. In fact, it seems that the less dust present, the greater the chance the subject has of developing Caplan's syndrome—a state of affairs which is difficult to reconcile with the above theory. Also, against this hypothesis is the fact that it is exceptionally rare to see peripheral rheumatoid nodules on the elbow or elsewhere in the absence of marked rheumatoid arthritis and, moreover, the appearance of such nodules in established systemic disease usually heralds an exacerbation. As already indicated, the pulmonary nodules of Caplan's syndrome often occur in the absence of overt rheumatoid arthritis. Even in those subjects who have long-standing joint disease and concomitant pulmonary nodulation, they by no means always indicate the advent of an exacerbation. Moreover, the Caplan nodule occurs much more commonly than does the necrobiotic nonpneumoconiotic pulmonary nodule. Thus it seems that, if the lesion is really just a modified necrobiotic nodule, the inhalation of dust not only modifies its character but also predisposes to its formation.

5. THE ASSOCIATION OF PROGRESSIVE MASSIVE FIBROSIS (CONGLOMERATION) AND RHEUMATOID ARTHRITIS

It has been shown that rheumatoid arthritis occurs more frequently in coal miners with progressive massive fibrosis than it does in the general population. The roent-genologic appearance of progressive massive fibrosis when it occurs concomitantly with rheumatoid arthritis in no way differs from that found in progressive massive fibrosis alone.

SUMMARY

This review calls attention to the pulmonary manifestations of rheumatoid arthritis. These are more common than is supposed and often remain unrecognized because of their protean character. If the possible cause and effect relationship be-

tween rheumatoid arthritis and an abnormal chest roentgenogram is borne in mind, the diagnosis of rheumatoid lung would be made more frequently and perhaps a few unnecessary diagnostic thoracotomies would be avoided.

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We are indebted to Dr. A. Schubart, Head of the Division of Arthritis, for arranging to have the latex fixation tests performed. We are also grateful to the Editor of *Thorax* for kindly allowing us to reproduce Figure 11.

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PULMONARY PARENCHYMAL FINDINGS IN BLUNT TRAUMA TO THE CHEST*

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WITH the increased rate of automobile accidents during the recent years, more blunt trauma to the patient's chest has been encountered in the general hospital than ever. Two hundred cases of patients who sustained blunt trauma to the chest were reviewed and all were found to have parenchymal changes. Ninety-four per cent of the cases had rib fractures, indicating that the trauma was of a moderately severe nature; 68 per cent of the cases, in addition to having rib fractures, also had associated pneumothorax or hemothorax. In this study attention was directed only to the type of parenchymal involvement present.

The parenchymal changes in blunt trauma to the chest have been attributed to the transmission of force to the underlying lung by tissues of the thoracic cage, by compression and recoil phenomena of the lung, and by reflex mechanism. The parenchymal changes encountered comprised: (1) pulmonary edema and congestion, (2) atelectasis, (3) patchy infiltrations, and (4) formation of traumatic lung cavities and intrapulmonary hematoma. Often a combination of the above mentioned changes was noted on a single chest roentgenogram. Usually, one type predominated.

ANIMAL EXPERIMENT

Our interest in the roentgen findings of pulmonary contusions prompted us to do the following experiment. A dog, weighing 20 kg., was used for the experiment of blunt trauma to the chest. The dog was anesthetized and open thoracotomy was performed on the right. The right lung was then contused with noncrushing, intestinal rubber shods, the thoracotomy incision closed and the lung re-expanded. Two

hours later the dog was sacrificed and the thoracic contents were removed en bloc. On gross pathology the contused right lung was markedly boggy, edematous, and discolored (Fig. 1). There were areas of subpleural hemorrhage. A roentgenogram of the inflated lung showed varying sizes of traumatic lung cavities from rupture of the alveoli and, also, diffuse, hazy densities, representing areas of intra-alveolar, perivascular and peribronchial hemorrhage (Fig. 2). Due to the elastic recoil phenomenon of the alveoli,7 the ruptured or lacerated alveoli assumed oval or rounded shape. When these lacerated alveoli were filled with air, or partly filled with liquid blood, the appearance was that of a traumatic lung cavity. When they were completely filled with blood, the shape and appearance resembled pulmonary hematomas. The microscopic appearance of the sections of the representative areas of the contused

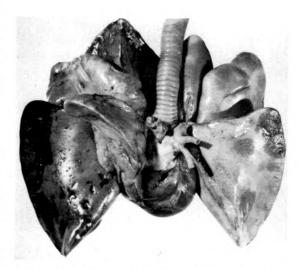


Fig. 1. The contused right lung of the dog is markedly boggy and discolored with numerous areas of subpleural hemorrhage. The left lung is normal.

^{*} From the Department of Radiology, Wayne County General Hospital, Eloise, Michigan.

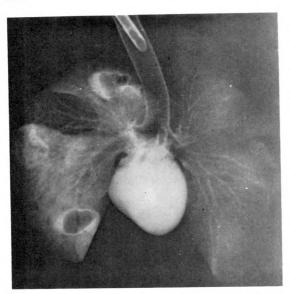


Fig. 2. Roentgenogram taken of the inflated lungs shown in Figure 1. The contused right lung shows various areas of traumatic cavities from ruptured alveoli. Note also patchy areas of density due to intra-alveolar hemorrhage.

lung of the dog revealed areas of intraalveolar hemorrhage, edema, beginning formation of hematoma and congestion.

ROENTGEN FINDINGS

In the present series about 15 per cent of the cases showed roentgenographic changes of acute parenchymal edema and congestion. This type of change, as described by Daniel and Cate,2 is due to the presence of edema fluid by dilated extravascular and lymphatic spaces and the presence of fluid within the alveoli and bronchioles. Their experimental study favors neurogenic factors of reflex mechanism through sympathetic nerve supply. Arteriole and capillary dilatation has been described by Falla4 in his microscopic study. These roentgen changes usually clear up within 24 hours if, in the meantime, no other complications develop. Figure 3 shows the appearance of acute edema and congestive changes.

Atelectasis was demonstrated in 16 per cent of the series. In most cases the atelectasis was not present on the initial roent-genogram, rather it was observed on the chest studies made 1 to 2 days after the

initial trauma. The mechanism of atelectasis, as described by DeTakats *et al.*, consists of obstruction of the bronchus with massive secretion, insufficient movement of the cilia and suppressed cough mechanism. The atelectasis can also be caused by obstruction of the bronchus due to blood clots or peribronchial hemorrhage. Ruptured bronchus, as described by Williams and Bonte, as a rare cause of atelectasis, and we have not encountered such an instance in our series. The atelectatic changes usually follow a segmental distribution. The atelectasis may persist for as long as 2 months.

In about 69 per cent of the cases reviewed, the predominant roentgen findings consisted of patchy, mottled, irregular, ill-defined densities on the initial chest roentgenograms. This roentgen appearance cor-

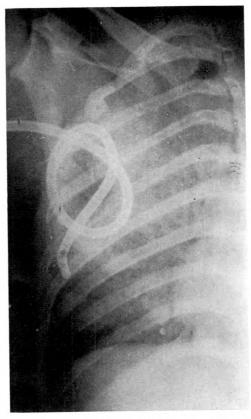


Fig. 3. Roentgenogram illustrating the appearance of acute edema a few hours following blunt trauma to the chest.

relates with the microscopic findings of perivascular, peribronchial and intra-alveolar hemorrhage and transudate. These changes often occurred on the same side as the blunt trauma to the chest; they usually cleared up in a few days to 2 weeks. However, there were 15 cases (about 7 per cent) which showed formation of traumatic cavities and intrapulmonary hematoma. The intrapulmonary hematoma can persist in the chest roentgenogram for a period of 2 to 10 months.

A few cases are presented briefly to illustrate the appearance of traumatic cavities and intrapulmonary hematomas.

ILLUSTRATIVE CASES

Case I, #141523. The initial roentgenograms of this patient, following an automobile accident, revealed patchy, ill-defined densities in the right upper lobe due to peribronchial, perivascular, intra-alveolar hemorrhage and transudate (Fig. 4). A roentgenogram made I week later demonstrated clearing of the patchy densities and an air fluid level in the traumatic cavities. This contained liquid blood and

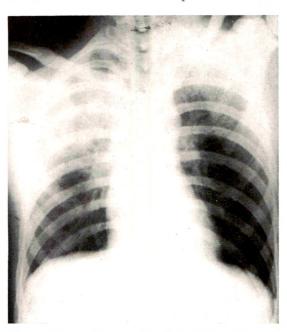


Fig. 4. Case I. Note the localized, ill-defined densities in the right upper lobe at the site of the blunt trauma. This roentgen appearance correlates with microscopic findings of peribronchial, perivascular and intra-alveolar hemorrhage and transudate.

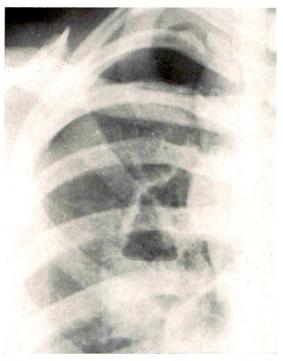


Fig. 5. Case I. Roentgenogram made I week later shows clearing of the hazy densities but now there is formation of a traumatic cavity containing liquid blood and trapped air.

trapped air (Fig. 5). Chester¹ demonstrated in his case that such traumatic cavities have no connection with the bronchial tree. The air in the traumatic cavities probably represents trapped air in the alveoli. One month later the air had completely resolved and a marked decrease in the size of the traumatic cavity with formation of an intrapulmonary hematoma was noted (Fig. 6).

Case II, #125504. The initial admitting chest roentgenogram of this patient, following an automobile accident, demonstrated ill-defined densities in the right lung (Fig. 7). Two weeks later there was clearing of the densities and a slightly oval, more discrete, soft tissue density in the right lower lobe (Fig. 8). This probably represents the beginning of intrapulmonary hematoma formation. The patient was lost to follow-up until 3 months later. He returned to the hospital after being rejected for employment because of findings on a pre-employment chest roentgenogram. He was told that he had a tumor of the lung. A chest roentgenogram showed a very discrete, sharply circumscribed, intrapul-



Fig. 6. Case I. Roentgenogram obtained I month later shows marked decrease in the size of the traumatic cavity with complete resorption of air and formation of an intrapulmonary hematoma.

monary hematoma in the right lower lobe (Fig. 9). No calcification was present. In the light of the previous trauma and serial chest studies, a diagnosis of intrapulmonary hematoma was made and a thoracotomy was averted. Six months later the follow-up chest roentgenogram showed further decrease in the size of the hema-

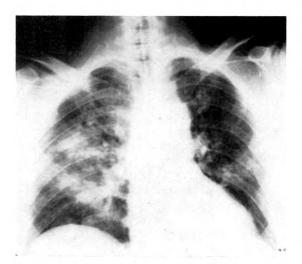


Fig. 7. Case II. Admitting chest roentgenogram shows patchy density in the right lung on the side of the blunt trauma.

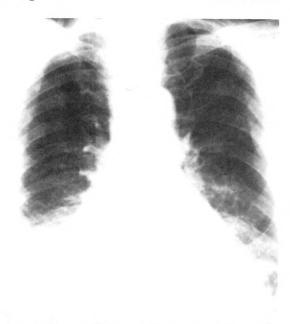


Fig. 8. Case II. Chest roentgenogram made 2 weeks later shows an oval density in the right lower lobe, representing intrapulmonary hematoma.

toma (Fig. 10). A 1 year follow-up chest roentgenogram demonstrated complete clearing of the hematoma.

Case III, #93379. The initial chest study of this patient showed a patchy density in the



Fig. 9. Case II. Roentgenogram made 3 months later. Note considerable decrease in the size of the intrapulmonary hematoma. The intrapulmonary hematoma appears sharply circumscribed. No calcification is present.

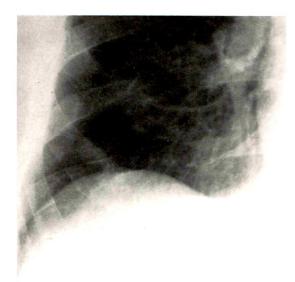


Fig. 10. Case II. Follow-up chest roentgenogram made 6 months later shows further decrease in the size of the intrapulmonary hematoma.

right lung with a suggestion of an area of radiolucency in the center of the density, probably representing the site of alveolar laceration (Fig. 11). Roentgenograms made 4 days later showed clearing of the patchy density, but then revealed a slightly lobulated soft tissue density in the right upper lobe (Fig. 12). On the followup study I week later, the presence of a thick-

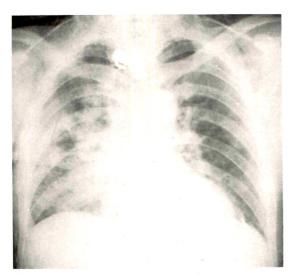


Fig. 11. Case III. Admitting chest roentgenogram shows patchy density in the right lung. Note also the presence of subcutaneous emphysema. Among the densities of the right upper lobe, there is an area of radiolucency, probably the site of alveolar laceration.

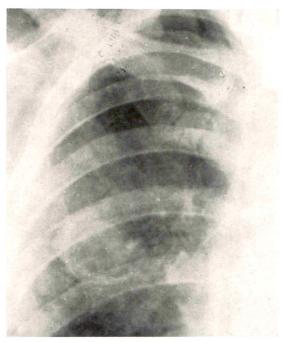


Fig. 12. Case III. Follow-up chest roentgenogram made 4 days later shows clearing of the patchy densities. A lobulated, more defined density in the right upper lobe suggests formation of a traumatic cavity.

walled traumatic cavity and also a small intrapulmonary hematoma behind the traumatic cavity was noted (Fig. 13). The wall of this cavity appeared slightly irregular in outline. This would be difficult to differentiate from abscess or necrotic neoplasm without serial roentgenography. One month later the chest roentgenogram showed further decrease in the size of the traumatic lung cavity and the hematoma (Fig. 14).

Case IV, #127612. In this case, the initial roentgenogram of the chest revealed a hazy irregular density in the left lung (Fig. 15). A follow-up study 4 days later demonstrated a discrete, sharply outlined, subpleural, intrapulmonary hematoma (Fig. 16). A roentgenogram made 2 weeks later showed further decrease in the size of the hematoma. Oblique roentgenograms demonstrated the subpleural location of this hematoma. Complete clearing resulted 2 months after the initial trauma.

DISCUSSION

In this study, the importance of obtaining, at the earliest possible moment, chest



Fig. 13. Case III. Follow-up chest roentgenogram made I week later reveals the presence of a well defined, thick-walled, traumatic cavity. Note that the wall appears slightly irregular in outline.



Fig. 14. Case III. One month later, a follow-up roentgenogram shows further decrease in the size of the traumatic cavity.

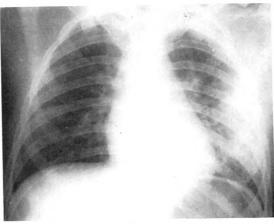


Fig. 15. Case IV. Admitting chest roentgenogram shows increased haziness of the left lung following an automobile accident.

roentgenograms after moderately severe blunt trauma to the chest is stressed. The follow-up chest roentgenograms, 24 to 48 hours later, are pertinent in detecting late atelectatic changes or the clearing of edema, or the development of pneumothorax or hemothorax. Follow-up chest roentgenograms in I and 2 weeks are of value, inasmuch as most of the cases reviewed showed that the density caused by intra-alveolar, peribronchial hemorrhage usually cleared up by that time. In the case of hematoma formation, follow-up chest roentgenograms should be obtained at I month, 3 month, 6 month and I year intervals.



Fig. 16. Case IV. Roentgenogram made 4 days later reveals a sharply outlined subpleural intrapulmonary hematoma.

In 200 cases reviewed, the most prevalent roentgen parenchymal findings were the changes caused by intra-alveolar, peribronchial and perivascular hemorrhage. In patients showing traumatic cavities with intrapulmonary hematomas, the differential diagnosis from abscess, granuloma or neoplasm would be difficult if serial chest roentgenograms and history were not available. In this series, all of the cases (7 per cent) showing traumatic cavities and pulmonary hematomas demonstrated definite decrease to complete clearing of the lesions on follow-up studies.

SUMMARY

Chest roentgenograms of 200 patients who sustained blunt trauma to the chest were reviewed.

The pulmonary roentgen findings consisted of edema and congestion, atelectasis, patchy hemorrhagic infiltration, formation of traumatic lung cavities, and intrapulmonary hematomas.

The importance of serial follow-up roentgenographic studies of the chest is stressed.

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ATRESIA OF THE BRONCHUS TO THE APICAL-POSTERIOR SEGMENT OF THE LEFT UPPER LOBE*

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A NUMBER of anatomic variations is encountered in the bronchial tree. Although the incidence of structural aberration is particularly high in the subsegmental bronchi of the left upper lobe, atresia of the bronchus to the apical-posterior segment is rare. Only 6 examples of this entity have been described in the medical literature. Recently, 2 patients in this institution were found to have this anomaly, and their cases form the subject of this report.

The abnormality was first reported by Belsey¹ in 1958. He observed that atresia was limited to a site near the origin of the major segmental bronchus. The more distal ramifications were patent, and the segment of lung served by these branches was emphysematous. These same morphologic features were noted in each of the patients discussed by Simon, Reid and Waddell.^{4,5} A similar structural pattern existed in the patients discussed below, thus marking the lesion as a distinct pathologic entity. Although this specific lesion is uncommon, it is important that the radiologist be aware of this; for the roentgenographic appearance is so distinctive that it provides strong presumptive evidence of the exact diagnosis.

REPORT OF CASES

Case 1. The chest roentgenogram of a 17 year old male in apparent good health demonstrated a mass in the left upper lobe. The lung adjacent to the mass appeared emphysematous. Two years later, although he still had no symptoms of pulmonary disease, the patient was advised to have the lesion removed. Thoracotomy revealed emphysema of the apical-posterior seg-

ment, and this portion of the lung was devoid of exogenous pigment.

The apical-posterior segmental bronchus was occluded near its origin. Beyond this point, the lumen was patent, but markedly distended by an accumulation of mucoid material. The dilated structure formed a mass, the roentgen image of which resembled a pulmonary nodule. Examination of the surgical specimen showed the distended portion of the lumen to measure 1×2 cm. It was filled with mucoid material. Peripherally, the small and medium sized bronchi were only slightly ectatic. The other segments of the lobe were normal. The roentgen manifestations of the lesion are shown in Figure 1, A and B.

Case II. The chest roentgenogram of a 3I year old pregnant woman demonstrated a discrete tumor mass in the left upper lobe. The lung adjacent to this rounded density appeared abnormally radiolucent, as if it were emphysematous. Drawing on the knowledge gained from Case I, a presumptive diagnosis of atresia of the apical-posterior segmental bronchus was made. Surgery was postponed until after delivery. During this interval, the patient was carefully observed, and studies made 4 and 6 months after the initial study demonstrated no change in the roentgenographic pattern (Fig. 2, A and B). The patient remained asymptomatic.

At thoracotomy, a thin sheet of tissue was discovered which completely obstructed the lumen of the apical-posterior segmental bronchus near its origin. Two areas of bronchial distention were encountered: one was adjacent to the obstruction, and the other more distal. The roentgenographic appearance of the lesion is shown in Figure 3, A and B. Detailed examination of the specimen revealed local emphysema, a lack of anthracotic pigmentation, a normal blood supply, and normal bronchi in the periphery of the segment. All these findings were similar to those encountered in Case I.

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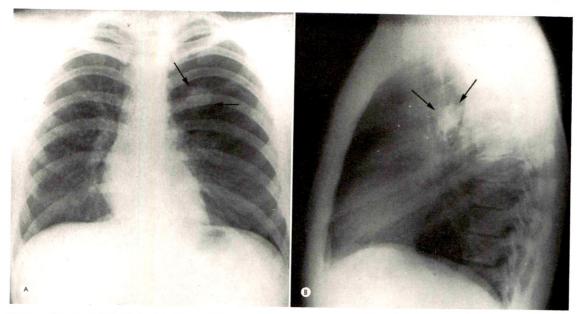


Fig. 1. Case I. (A) Posteroanterior and (B) lateral roentgenograms of the chest of a 17 year old male demonstrating the presence of a mass-like lesion in the left upper lobe (arrows) and obvious emphysema in a portion of the left upper lobe.

DISCUSSION

In the 2 examples of atresia of the bronchus to the apical-posterior segment of the left upper lobe which are reported here, like those previously described, localized oblit-

eration of the lumen of the segmental bronchial tree at a point near its origin constitutes the fundamental structural abnormality of the lesion. The peripheral branches within the pulmonary segment were patent

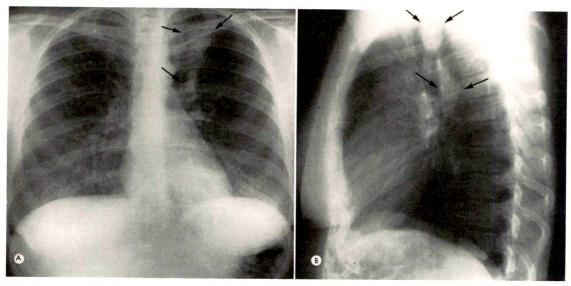


Fig. 2. Case II. (A) Posteroanterior and (B) lateral chest roentgenograms of a 31 year old female demonstrating the presence of emphysema in the left upper lobe and a large, smoothly marginated mass within the region of emphysema (upper arrows). The lower arrows point to the less well defined mass representing moderate cylindrical bronchial dilatation immediately adjacent to the point of obstruction of the apical-posterior bronchus.

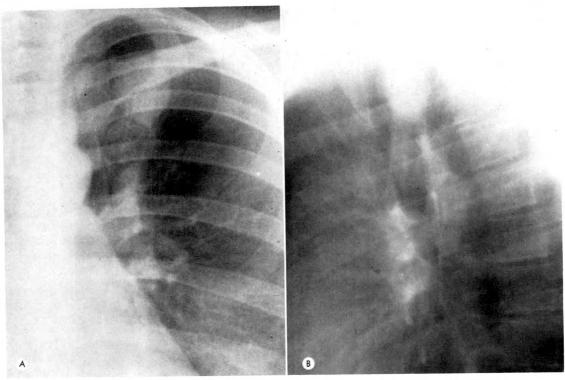


Fig. 3. Case II. (A and B) Enlarged roentgenograms of the area of interest to better illustrate the two mass-like lesions in the left upper lobe.

and appeared to have undergone normal embryologic development. Unlike the pattern in pulmonary sequestration, no evidence of an accessory bronchus nor of abnormal vasculature in the involved segment has been demonstrated.

Normal mucus-secreting glands within the bronchial epithelium, distal to the occlusion, elaborate fluid which causes spherical or cylindrical dilatation in portions of the obstructed bronchial segment. The ectatic changes produced by this mechanism sometimes have the roentgenographic characteristic of a soft tissue mass. In both of the cases cited here, there was slight dilatation of the bronchus immediately beyond the point of obstruction, as well as a larger, very sharply defined mass within the emphysematous segment. However, the roentgen pattern produced by the dilated bronchus may vary. The homogeneous, sharply circumscribed lesion demonstrated in Figure 2, A and B; and 3, A and B resembles a solid mass, but mucus-distended bronchi were not present in all the previously reported cases, and it would appear that the amount of liquid in the occluded bronchus and the resultant bronchial dilatation vary with the rate of intraluminal mucus secretion. In I earlier report roentgen evidence of both liquid and air, contained within a 2 cm. ring-like shadow surrounded by emphysematous lung, was described.⁴

It is important to note that local emphysema is the feature common to all cases. Emphysema evolves during the early years of life. Air enters the segment normally served by the occluded bronchus via small anomalous communications which exist between the distal bronchioli in adjacent normal lung and the alveoli in the abnormal segment. This form of collateral ventilation does not permit the discharge of air to occur as rapidly or as completely as it does in a normal region. Thus, the segment becomes pathologically distended and emphysema supervenes. During surgery,

the diseased segment is easily distinguished from the adjacent normal lung by its emphysematous appearance and the striking paucity of anthracotic pigmentation.

Obstruction of the bronchus serving the emphysematous segment may be demonstrated by bronchography, which also serves to differentiate the local parenchymal radiolucency which accompanies congenital bronchial atresia from the common form of regional emphysema caused by chronic bronchial disease acquired later in life.

The cause of congenital bronchial atresia is not known. Several interesting possibilities are suggested. It would appear that this lesion develops late in fetal life, after a normal airway has been formed. What effect bronchial artery occlusion has in embryonic life is not yet known but enteric atresia caused by mesenteric vascular occlusion in intrauterine life has been described, and a similar mechanism may affect the respiratory system. The observed high incidence of anatomic variation in the left upper lobe bronchi suggests the presence of an underlying embryologic instability; the possibility that bronchial atresia in this area represents some specific genetic abnormality is an interesting hypothesis. Because of the detailed study of the embryology and development of the bronchial tree by Boyden² and Bucher and Reid,³ the time at which atresia develops can be estimated. Segmental bronchi begin to appear in the embryo between the 30th and 34th day of development. By the 40th day, virtually all of the subsegmental bronchi have evolved, and by the 15th week of intrauterine life, the complete adult complement of intrasegmental bronchi in the left upper lobe is present. Thus, it would seem that the process which causes fetal occlusion near the origin of the segmental bronchus must occur after the 15th week, for the bronchial radicals distal to the zone

of atresia have appeared fully developed and morphologically normal in all the cases observed.

SUMMARY

Two cases of atresia of the apical-posterior bronchus of the left upper lobe are reported. Roentgenograms show emphysema of the left upper lobe. Slight distention of the bronchus by mucus immediately beyond the point of atresia and the presence of an oval, mall-like lesion are characteristic and were roentgenographically demonstrable in both cases. The bronchi distal to the area of atresia are normal in distribution. The condition can be recognized roentgenographically; bronchography is necessary if the characteristic bronchial distention and "mass" are absent.

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INFANTILE LOBAR EMPHYSEMA*

REPORT OF TWO CASES WITH UNUSUAL ROENTGENOGRAPHIC MANIFESTATION

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INFANTILE lobar emphysema is a well recognized cause of respiratory distress in infancy in which prompt recognition followed by surgical extirpation of the involved lobe results in cure of the patient. The preoperative diagnosis of infantile lobar emphysema is made by plain roent-genograms of the chest. The characteristic finding is that of an emphysematous lobe compressing and displacing adjacent structures. Of 4 patients with this disorder seen at this institution in the recent past, the roentgen manifestations were atypical in 2; these 2 cases form the basis of this report.

REPORT OF CASES

CASE I. D.M., a 2 day old white male, was admitted to Indiana University Medical Center with a history of dyspnea and cyanosis since birth. The right hemithorax was hyperresonant compared to the left side, and breath sounds were decreased on the right. Admission roentgenogram of the chest (Fig. 1) showed the mediastinum and heart to be displaced to the left, and there was separation of the ribs on the right. A wedge-shaped density was noted in the mid-portion of the right lower lung field. The major portion of the right lung had a hazy appearance with poor definition of the vascular markings. On the lateral roentgenogram, herniation of right lung across the anterior mediastinum was seen (Fig. 2). A diagnosis of infantile lobar emphysema was made, and after 12 hours of observation, thoracotomy was performed. The right middle lobe herniated through the surgical incision, and it was noted to occupy most of the pleural cavity, compressing the upper and lower lobes. A right middle lobectomy was performed, following which the patient made an uneventful recovery.

On gross examination of the right middle lobe, no abnormality of the bronchi was noted. The lung was subcrepitant. On microscopic exam-

ination the bronchi, bronchioles, and alveoli in many areas contained pale, eosinophilic material, indicating the presence of protein-containing fluid. An occasional squame was seen in this material. No abnormality of the cartilages was noted. In many foci, the alveoli were distended and there was rupture of the septa, producing large, cyst-like spaces.

Case II. D.S., a 2 day old white female, was referred to Indiana University Medical Center with a history of cyanosis and dyspnea of 24 hours' duration. Physical examination showed a dyspneic and cyanotic child with decreased breath sounds and increased resonance in the right chest. Initial chest roentgenogram (Fig. 3) demonstrated a shift of the heart and mediastinum to the left, with a wedge-shaped density in the right lower lung field. The remainder of the right lung was characterized by a hazy density obscuring the vascular markings. Hernia-

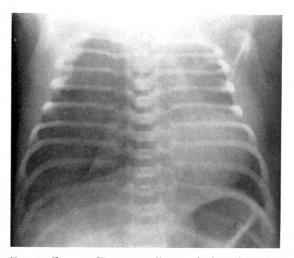


Fig. 1. Case 1. Pressure effects of the distended right middle lobe are evident, with collapse of the right lower lobe and shift of heart and mediastinum to the left. The right middle lobe fills the right hemithorax and shows a hazy density with obliteration of the normal vascular markings.

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Fig. 2. Case I. Herniation of the distended lobe through the anterior mediastinum is seen.

tion of the right lung through the anterior mediastinum was noted on the lateral roent-genogram (Fig. 4). Experience with Case I prompted the diagnosis of infantile lobar emphysema. At the time of thoracotomy, 8 hours after admission, the right upper lobe was found to be markedly emphysematous, compressing the adjacent lobes, and occupying almost the

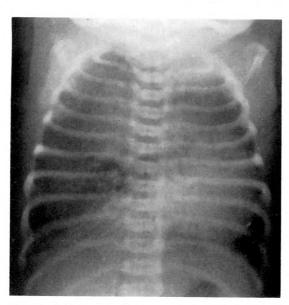


Fig. 3. Case II. The distended right upper lobe produces collapse of the middle and lower lobes and shift of the mediastinum to the left. The poor definition of vascular markings and hazy density are seen in the emphysematous right upper lobe, which fills the right hemithorax.



Fig. 4. Case II. The emphysematous right upper lobe herniates through the anterior mediastinum on the lateral roentgenogram.

entire pleural cavity. The surgeon commented that considerable fluid was present in the distended lobe. After lobectomy, the patient's postoperative course was complicated by intermittent atelectasis of portions of the lower lobes, but she eventually recovered completely.

On gross examination, the right upper lobe was noncrepitant, and clear yellow fluid exuded from the cut surface. No abnormality of the bronchi was seen. Microscopic examination revealed areas of emphysema interspersed with small foci of atelectasis. In the emphysematous areas, the alveoli were markedly distended and in many places the alveolar septa were disrupted, forming cyst-like spaces. The alveoli and bronchioles contained eosinophilic material with many squames, indicating the presence of protein-containing fluid (Fig. 5, A and B).

DISCUSSION

Infantile lobar emphysema is an occasional cause of respiratory distress in infancy; 26 cases have been encountered in a

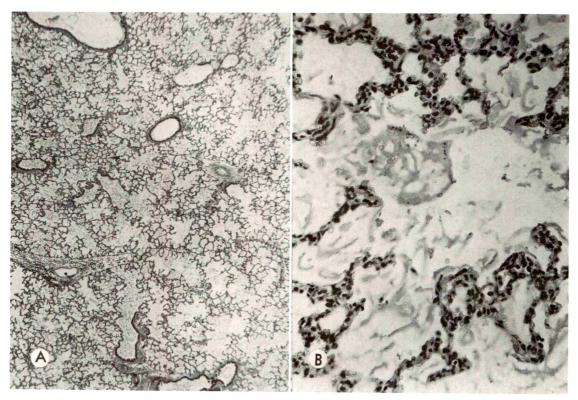


Fig. 5. Case II. (A) Emphysema with rupture of alveolar walls and protein-containing material in the bronchioles and alveoli (\times 20 magnification). (B) Note the emphysema, squames, and protein-containing fluid in the alveoli (\times 200 magnification).

10 year period in one large pediatric institution.⁵ About one-half of the patients present with the signs of respiratory distress in the neonatal period. The remainder are seen in the first to fourth month of life, and in these patients, symptoms are less severe. In the neonate, dyspnea with or without cyanosis is the presenting feature. The emphysema almost always involves a single lobe, usually the right or left upper or the right middle lobe.

Examination of the resected lobe reveals distention of the alveoli with rupture of alveolar walls and cyst-like formation. The etiology of infantile lobar emphysema is thought to be due to a ball-valve type of obstruction of the bronchi. The bronchial obstruction may be extrinsic, due to a patent ductus arteriosus, aberrant vessel, and enlarged heart or lymph nodes. Intrinsic bronchial obstruction may be caused by a deficiency of bronchial cartilage, bronchial stenosis, and redundant bronchial

mucosa.⁵ Several cases have shown only alveolar fibrosis, and this is thought by some to be the etiology of the emphysema.² In many instances, no specific anatomic abnormality is found,⁷ as in the 2 cases reported here.

Differential diagnosis includes congenital and postinfectious cysts, congenital adenomatoid hyperplasia, atelectasis with compensatory emphysema of remaining lobes, endobronchial foreign body, and diaphragmatic hernia.

Treatment of infantile lobar emphysema consists of surgical removal of the involved lobe. Surgery should not be delayed in those patients presenting in the neonatal period, as deterioration in the clinical status of the patient is frequent, and conservative treatment without lobectomy is usually fatal.

The typical roentgenographic manifestations of infantile lobar emphysema have been described in the literature;^{3,4,6} they

can be divided into signs of a distended lobe and signs of pressure effects on adjoining viscera. The involved lobe is enlarged, attenuation of vascular markings is present, and hyperlucency is noted. Pressure phenomena include collapse of adjacent lobes, shift of heart and mediastinum to the opposite side, depression of the diaphragm, separation of the ribs, and herniation of lung into the anterior mediastinum. The 2 cases reported here showed the typical pressure effects, with shift of the mediastinum and collapse of adjacent lobes. The unusual and noteworthy feature is that in each case the lobe was not radiolucent, but rather a hazy density was recognized with poor definition of the vascular markings. This is believed to be due to fluid accumulation in alveoli of the affected lobe. The origin of the fluid in these lobes is speculative. The presence of a large number of squames in Case II suggested aspiration of amniotic fluid at the time of delivery. In Case I only an occasional squame was seen, and this is not unusual in a newborn infant. Delayed absorption of the alveolar fluid found in fetal lungs is another possibility. Recently, Allen et al.1 reported a similar case in which they noted dilated lymphatic channels in septa of the lung. The microscopic slides in our cases did not show these lymphatics.

It is of some interest that of the 4 cases we have personally encountered, the 2 who presented in the neonatal period had edematous lobes, both roentgenographically and pathologically. Lucent, air-filled lobes typical of lobar emphysema were found in the patients whose onset of symptoms was late. Further experience is necessary to determine if this is of real significance.

As a result of experience with these 2 cases, we suggest that the diagnosis of infantile lobar emphysema should be considered in infants with respiratory distress if roentgenographic signs of an overexpanded lobe are present, even in the absence of hyperlucency of the lobe.

SUMMARY

Recognition of infantile lobar emphysema as the cause of respiratory distress in infancy is primarily a problem of roentgen diagnosis. Roentgen examination of the chest reveals a distended lobe compressing adjacent lung and displacing the heart and mediastinum to the opposite side. Two cases of infantile lobar emphysema are reported in which the emphysematous lobe was fluid-filled, causing a hazy density in the involved area on the chest roentgenogram. The origin of the fluid is not determined, but aspiration of amniotic fluid is considered as a possibility. The roentgen diagnosis of infantile lobar emphysema should be based on signs of overdistention, not hyperlucency of the lobe.

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ASPHYXIATING THORACIC DYSTROPHY OF THE NEWBORN*

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ASPHYXIATING thoracic dystrophy of the newborn is a rare, familial malformation with an early onset of respiratory distress and in many instances a fatal outcome. It was first described by Jeune et al.⁵ in 1955. The thoracic dystrophy is only one manifestation of a generalized chondrodystrophy, but since thoracic changes constitute the most salient feature of the disease and since pulmonary complications are the usual cause of death, this descriptive name used by Jeune and his co-workers appears to be an appropriate one.

There are 7 cases of this disease previously reported in the French and Italian literature. Recently, we have had the opportunity to observe a little girl presenting characteristic findings of asphyxiating thoracic dystrophy. She has been studied extensively, including a chromosomal analysis which has not been done before in patients with this condition. A review of the patients who have presented with atypical chondrodystrophies in the past years yielded 4 more cases; 3 of them were hospitalized between the years of 1956 and 1959.

Following is the presentation of our 5 cases and a brief discussion of the disease.

REPORT OF CASES

Case I. A.A.C. This 5 week old girl was admitted to Children's Hospital Medical Center because of "blue spells." The child weighed 2.4 kg. at birth and was kept in an incubator with oxygen for 4 days following delivery.

On admission she weighed 2.3 kg. and the length, head circumference and weight were below the third percentile. She was an oddly shaped baby with relatively short extremities and a long trunk. She was breathing rapidly and had expiratory wheezes and intercostal retrac-

tion. The extremities and lips were slightly cyanotic. There were 6 digits on each of the hands and feet. Physical examination was otherwise negative.

Routine urinalysis, blood cell counts and serum chemistries were negative. The urinary mucopolysaccharide level was normal, as was a chromosomal analysis.

Roentgen Findings. The thorax was grossly abnormal in contour with marked narrowing in its transverse and sagittal axes, accompanied by relative elongation of the vertical axis. The ribs were short and stubby with their underdeveloped distal ends hardly extending beyond the anterior axillary line. The distal costal metaphyses were swollen and revealed some splaying. The clavicles were abnormally high (Fig. 1, A and B).

In the pelvis, the iliac wings were short and had a squared appearance. The margins of the acetabular fossae and the triradiate cartilage areas showed marked irregularity and presented a scalloped outline (Fig. 2).

The long bones of the extremities were somewhat short and stubby but otherwise appeared unremarkable. Supernumerary fingers and toes were present. Roentgen examination of the skull and spine was within normal limits.

The child was treated with oxygen and developed atelectasis of the left lung with increase in her respiratory distress while in the hospital. There was gradual resolution of the atelectasis and she was weaned from oxygen. The baby was doing fairly well when she was discharged to the care of the parents, 14 days after admission.

Case II. R.C. This baby boy was admitted to the Children's Hospital Medical Center at I month of age with the chief complaints of cyanosis and jaundice. Cyanosis was noticed following delivery and onset of jaundice at 24 hours of age. He was placed in oxygen for 2 days following delivery.

On admission, the chest was noticed to be small and the abdomen was large and bulging. There was minimal beading of the costochon-

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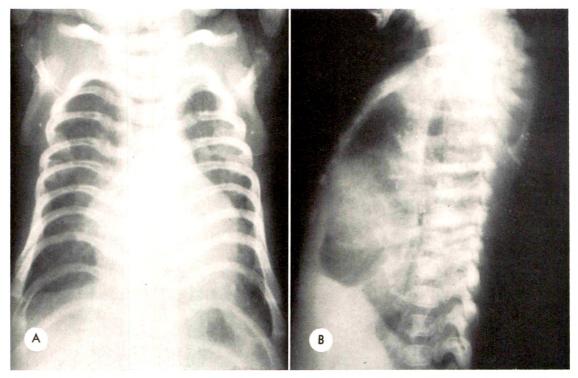


Fig. 1. Case I. (A) Posteroanterior and (B) lateral roentgenograms of the chest. Notice the markedly hypoplastic and short ribs which are terminating laterally with their ends barely showing on the posteroanterior roentgenogram. The anterior chest wall is abnormally high with the ribs retaining a horizontal position and the clavicles being abnormally high. The spine appears normal.

dral junctions. Otherwise, the physical examination was normal.

The abnormal laboratory data consisted of high levels of direct and indirect bilirubin in the blood (5.4/9.7 mg. per cent), decreased stool



Fig. 2. Case I. Roentgenogram of the pelvis. Abnormal and retarded enchondral ossification at the triradiate cartilage has resulted in hypoplastic iliac bones and irregular acetabular margins.

urobilinogen, and positive urine urobilinogen.

Roentgen Findings. The thorax was narrow and elongated with short and hypoplastic ribs displaying irregular and wide anterior metaphyses. The clavicles had a high position (Fig. 3, A and B; 4; and 5).

After discharge from the hospital this baby was followed at regular intervals in the out-patient clinic and was treated for frequent respiratory infections. He died at 11 months of age.

Our next 3 patients (P.McC., R.McC., and B.McC.) are siblings. There are 2 more siblings in this family and they are normal. The mother of the children is normal, whereas the father has dorsal spine changes which are thought to be residual deformities of Scheuermann's disease. One paternal aunt is known to have died in infancy of pneumonia.

Case III. P.McC. This was the first Children's Hospital Medical Center admission of this 26 month old white male with cough and fever. The patient was born with an abnormally





Fig. 3. Case II. (A) Posteroanterior and (B) lateral roentgenograms of the chest.



Fig. 4. Case II. Roentgenogram of the pelvis. The iliac bones are very small; the hypoplastic iliac wings are squared. The deep sciatic notches resemble those of an achondroplastic pelvis but there is no narrowing of the lumbar interpediculate spaces.

shaped chest and has been having multiple episodes of upper respiratory tract infections often associated with otitis media. His growth rate throughout has been slow.

Physical examination revealed rather short extremities and the external manifestations of the chest deformity were seen in the roentgenograms of the chest (Fig. 6, A and B).



Fig. 5. Case II. (A and B) Roentgenograms of the upper extremities. The metaphyses are widened and the physes are very irregular and present a scalloped profile, reflecting the disturbed enchondral ossification.

The patient was found to have bronchopneumonia and after 2 days of treatment was discharged with improvement.

Laboratory data including a chromosomal analysis and urine mucopolysaccharide determination were normal.

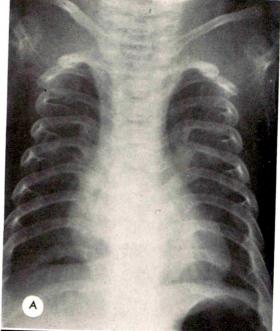
Case IV. R.McC. This elder sibling in the same family was first seen in the Children's Hospital Medical Center as an outpatient at 2 years of age with bronchitis and a chest deformity. His recurrent respiratory tract infections before and after this episode were treated by his pediatrician, and, at the time of his younger sibling's hospitalization 7 years later, he was brought into the Children's Hospital Medical Center for a follow-up. His early severe thoracic deformity revealed remarkable improvement over this period of 7 years and this interesting sequence is shown in Figures 7, A and B; and 8, A and B.

Case v. B.McC. This youngest sibling in the McC. family was 2 years old at the time the entire family was brought to Children's Hospital Medical Center for examination (November, 1965). Following birth, he suffered from recurrent respiratory tract infections quite similar to those of the affected siblings and these were treated by the same family physician.

Roentgen examination of the chest and pelvis revealed chondrodystrophic changes identical to the ones seen in his elder brothers (Fig. 9, A and B; and 10).

DISCUSSION

A review of the reported cases of this polychondrodystrophy shows that the degree of involvement of different parts of the fetal skeleton is quite variable. One constant and unifying finding in all the patients is the marked thoracic deformity. The disturbed ossification in the costochondral junctions leads to abundant irregular cartilage growth, somewhat resembling a rachitic rosary, and to underdeveloped, short, stubby ribs. The result is a small, immobile thorax. Because of the hypoplastic fixed thoracic cage, respiratory motions are almost exclusively abdominal. Air exchange is very poor, and these patients are prone to recurrent pulmonary infections, asphyxia and death. In marked contrast to the recessed chest wall, the



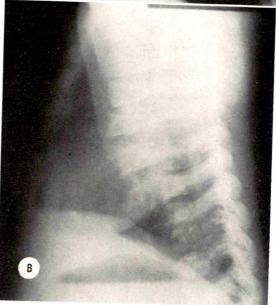
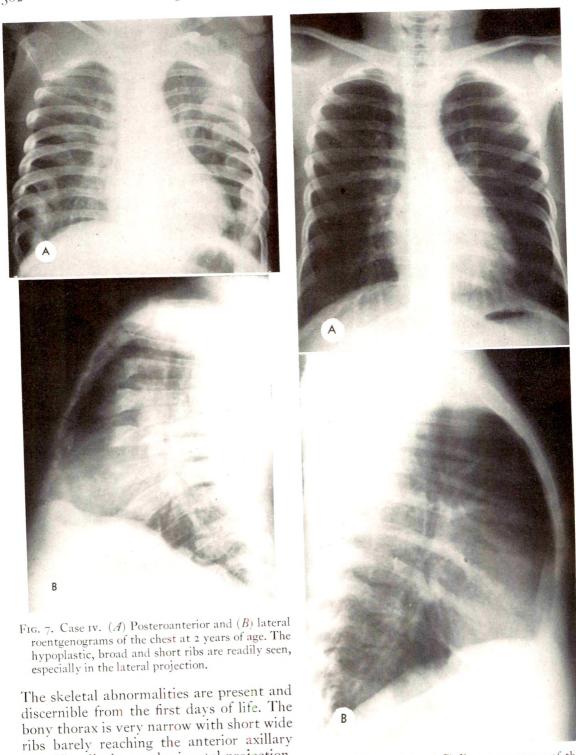


Fig. 6. Case III. (A) Posteroanterior and (B) lateral roentgenograms of the chest, again showing the characteristic deformity with short and stubby ribs.

abdomen appears to be protruding and voluminous. Abdominal respirations are vigorous. Head shape is normal. The extremities may be short and stubby. Polydactyly has been observed in 3 patients.

Roentgenographic examination provides the most important clues to the diagnosis.



line. The ribs have a horizontal projection. The anterior chest wall and clavicles retain a fixed, elevated position. The distal costal metaphyses show some widening. The

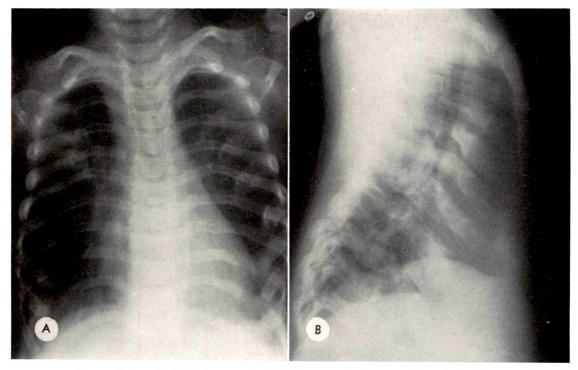


Fig. 9. Case v. (A) Posteroanterior and (B) lateral roentgenograms of the chest.

costochondral junctions are splayed and irregular. The heart may appear relatively enlarged because of the microthorax, but usually there is no true cardiomegaly. The pelvis is always small and the hypoplastic iliac wings have a squared appearance. Both the crest apophyseal edges of the ilia and the enchondral ossification margins around the triradiate cartilages are very irregular, often scalloped. The long bones of the extremities may be relatively short and wide. There may be disturbance of ossification in the metaphyses. However, the manifestations of this generalized osteochondrodystrophy are minimal in the extremities and much less obvious than in achondroplasia. The skull and spine are roentgenographically normal.

Several patients have died in the first or second year of life; survivors include I case reported by Neimann *et al.*, which was still alive at the age of 3, and 4 of our cases, one of which is only 9 months old now.

There is only one postmortem examination available in this group of patients.8

The microscopic examination of the costochondral junctions showed very disordered and poorly progressing enchondral ossification. The hyaline cartilage was normal. The proliferating cartilage was hyperplastic and very abundant. The zone of provisional calcification, however, remained very limited and vessels penetrated it irregularly.



Fig. 10. Case v. Anteroposterior roentgenogram of the pelvis showing the typical squaring of the iliac wings.

The continuity between the cartilage columns and bone was irregular and abnormal. The nodular hypertrophy at the costochondral junctions was caused by proliferation of cartilage and by deposition of a disordered fibrocollagenous tissue.

With complete roentgenographic examination of the skeleton, asphyxiating thoracic dystrophy can usually be easily differentiated from achondroplasia, epiphyseal dysplasia and metaphyseal dysostosis. Actually, the only disease to which it may bear a close resemblance is the Ellis-Van Creveld syndrome. The appearance of the pelvis is quite similar in both diseases. However, in the patients with the Ellis-Van Creveld syndrome, the involvement of the thorax in the chondrodystrophic process is minimal and, in most cases, the thorax is completely normal in the presence of definite changes in the long bones of the extremities. In addition, manifestations of ectodermal dysplasia, such as abnormal teeth and nails, in this latter group of patients are further helpful in differentiating them from our patients with the thoracic dystrophy.

Our fourth case suggests that the chondrodystrophic changes are reversible in later childhood. Extremely vigilant care is necessary to tide these patients over the respiratory complications of the critical first years of life.

SUMMARY

Asphyxiating thoracic dystrophy is a rare and in most instances fatal osteochondrodystrophy affecting the bony thorax. Patients with this syndrome have a small, immobile thorax, are prone to respiratory difficulties and may succumb to pneumonia and its complications. The smallness of the

thorax is mainly due to hypoplasia of the ribs. The long bones of the extremities are usually short and wide but are not severely affected.

Five cases of this osteochondrodystrophy are reported.

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We wish to thank Dr. Edward C. Dyer of Brookline, Massachusetts, for permitting us to include his patients in this study.

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PSEUDOVASCULAR RING RESULTING FROM RIGHT LUNG AGENESIS, NORMAL AORTIC ARCH, AND PATENT DUCTUS ARTERIOSUS

CASE REPORT

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AGENESIS of the lung is a rare anomaly with only 150 cases reported in the world literature.² The embryology and clinical manifestations of the unilateral absence of pulmonary structures have been thoroughly described elsewhere, and will not be discussed here.4,5,6

The purpose of the authors is to describe a previously unreported associated cardiovascular abnormality which hastened the patient's demise; that is, an anatomically complete pseudovascular ring which caused severe tracheal compression. The exact nature of this potentially correctable, lethal mechanism was not revealed until autopsy, but its recognition in future cases could have a vital influence on the patient's course.

REPORT OF A CASE

On admission to this institution, physical examination showed an active, slightly cyanotic, white female infant in moderate respiratory distress. There was hyperextension of the neck with persistent deviation of the head to the right. Although the neck was movable, flexion of the head caused an obvious increase in the respiratory distress. The chest was asymmetric with flattening of the right anterior rib cage. There was mild subcostal retraction with inspiration. Decreased breath sounds and dullness to percussion were noted over the right chest. The cardiac rhythm was normal. A soft, blowing, grade 3/6 holosystolic murmur was heard best over the right precordium, and radiated into the right axilla and back.

The electrocardiogram showed dextrocardia

with limb leads reversed. Initial roentgenogram showed the right hemithorax to be opaque, with shift of the mediastinum and heart into the right thoracic cavity. There was marked overexpansion of the left lung, suggesting the diagnosis of agenesis of the right lung. There were also rib anomalies, hemivertebrae from T-2 to T-II (Fig. I), and bilateral dislocated hips.

Several unsuccessful attempts were made to wean the infant from her high oxygen environment by decreasing the oxygen content of the



Fig. 1. Plain roentgenogram of the chest showing a marked mediastinal shift to the right. Absence of the right lung has allowed the heart to rotate horizontally into the right hemithorax. Vertebral anomalies are also visible.

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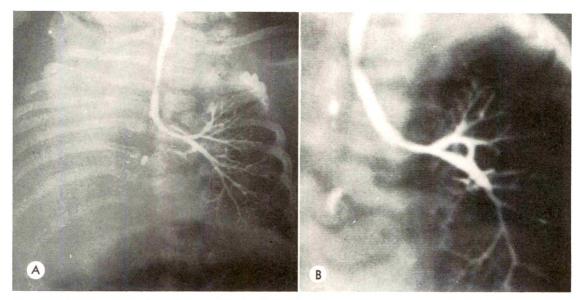


Fig. 2. (A) Antemortem bronchogram showing lack of pulmonary air passages on the right. (B) Magnified view of distal tracheobronchial area. No evidence of airway compression can be seen.

Isolette; however, this invariably resulted in deepening cyanosis and tachypnea within 4 or 5 minutes. Tracheal compression by a constricting vascular ring was suspected clinically. A subsequent bronchogram showed total absence of the right lung, but no tracheal compression (Fig. 2, A and B).

On the 11th hospital day, biplane and cine angiocardiography was performed after cardiac catheterization via the right saphenous vein. The biplane roentgenograms were not diagnostic because of persistent marked rotation of the patient, and no abnormalities of the circulatory system were apparent. Cine roentgenograms demonstrated dextroversion of the heart, absence of the right pulmonary artery, and questionable patent ductus arteriosus. There was no evidence of vascular anomalies to confirm the clinical impression of a constricting vascular ring. An esophagram was not remarkable.

On the 19th hospital day the patient had a seizure, and her condition deteriorated rapidly. Three days later she had several episodes of cyanosis. She expired the following day.

Roentgenograms taken after postmortem injection of contrast material into the main pulmonary artery showed absence of the right pulmonary artery and normal pulmonary vasculature on the left (Fig. 3).

Autopsy confirmed the suspected agenesis of the right lung. The heart was of normal external configuration but was twisted 90 degrees about its vertical axis and lay almost horizontally in the right thoracic cavity. The great vessels arose from their normal position and passed in the normal manner to the left and posterior to the trachea and esophagus. However, a large patent ductus arteriosus was stretched tightly across the left anterolateral side of the distal trachea which was severely compressed. There was also an anomalous left subclavian vein entering the left atrium and a pulmonary vein entering the right atrium.

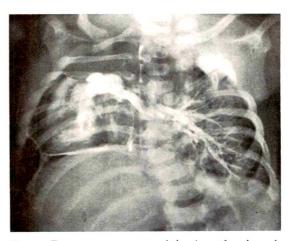


Fig. 3. Postmortem contrast injection of main pulmonary artery. There is absent pulmonary vasculature on the right, while that on the left appears to be normal.

DISCUSSION

Congenital absence of the lung has other associated anomalies in 50 to 60 per cent of the cases, of which about 25 per cent are vascular in origin. 1—4 Although patent ductus arteriosus is the most common of these vascular malformations, no case similar to the one presented here could be found in the literature. In fact, the described clinical effects of patent ductus in the presence of lung agenesis were the same as those seen in common patent ductus arteriosus alone.

It is pertinent to note that lung agenesis by itself is rarely symptomatic, and may be discovered only accidentally during routine examination. Thus, a congenitally absent lung may be important primarily as a medical curiosity. This fact should make the physician reluctant, as it did here, to ascribe severe respiratory distress solely to the lung anomaly, and other causes must be sought.

The clinical combination of persistent respiratory distress, hyperextended neck, and stridor upon head flexion suggested tracheal compression by an encircling vascular ring. The basic component of such rings is the abnormal placement of the aortic arch on the right side of the trachea; the left side of the ring is usually completed by a ligamentum arteriosum or patent ductus which passes from the displaced arch to a normal main pulmonary artery. Many variations of this arrangement have been described, but all true vascular rings have components on both sides of the trachea, and occasionally the esophagus is included as well. Since many such rings can be surgically corrected, that possibility justifies a vigorous diagnostic approach.

There was no reason to expect an abnormal esophagus since no vascular structures encircled or compressed it and the aortic arch was normal in appearance and location, as indicated above. The apparent absence of tracheal compression on the bronchographic films was subsequently explained. By duplicating the previous angle of the roentgenographic exposure while

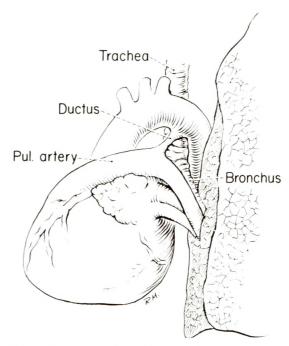


Fig. 4. Drawing of *en bloc* thoracic contents at autopsy. Total agenesis of right pulmonary structures, with cardiac dextroversion and horizontal displacement. Note distal tracheal compression by taut patent ductus arteriosus which acts as a *pseudo*vascular ring.

directly visualizing the bared thoracic contents during postmortem examination, the area of tracheal compression was seen to lie directly in the anteroposterior plane, and thus would have been obscured by the contrast medium behind it during the initial examination.

The mechanism of this pseudovascular ring was not complicated. When patchy areas of the left lung became atelectatic, overdistention of the aerated segments pushed the heart even further into the empty right hemithorax. This caused the taut patent ductus to press more firmly against the trachea, setting up a lethal cycle of compression-dyspnea-overexpansion.

The multiple defects and moribund condition of this infant precluded a favorable prognosis even if the ductus had been surgically corrected. However, the future recognition of this pseudovascular ring in a

more favorable case could initiate a life-saving course of corrective action.

SUMMARY

A case is described with clinical, roentgenographic and anatomic features of pseudovascular ring not previously reported in the literature. Early neonatal proof of a congenitally absent right lung did not explain the infant's respiratory distress, and the suspected tracheal compression could not be verified before her death in the 11th week. Postmortem examination disclosed that shifting of the heart into the right thoracic cavity had caused a patent ductus arteriosus to impinge on the distal trachea. The aortic arch was on the left as is normal. Although mimicking the signs and symptoms of a true vascular ring, this arrangement did not actually encircle the mediastinal structures.

It is postulated that awareness of this

entity will permit its early diagnosis in some future case, thus initiating a lifesaving ablation of the constricting ductus arteriosus.

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CALCIFICATION OF THE PULMONARY ARTERY AND ENLARGEMENT OF THE RIGHT VENTRICLE: A SIGN OF CONGENITAL HEART DISEASE*

EISENMENGER SYNDROME — PULMONARY HYPERTENSION, INCREASED PULMONARY RESISTANCE, AND REVERSAL OF BLOOD FLOW

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IN A recent communication, 4 women with calcification of the pulmonary artery due to reversal of blood flow through a patent ductus arteriosus were described, and it was emphasized that when calcification of the pulmonary artery was present, this sign should suggest such a diagnosis.5 Goldfischer,² in 1963, described calcification of the pulmonary artery in a 40 year old woman who had a ventricular septal defect, eccentric thickening of the intima of the smaller branches of the pulmonary artery, reversal of blood flow, and a closed ductus. Death was due to a brain abscess. Since then, 3 men, all with pulmonary artery calcifications, enlarged right ventricles, huge pulmonary arteries, and cardiac or aortopulmonary shunts with the clinical picture of the Eisenmenger syndrome⁹ have also been encountered at this center. One patient had dextrorotation of the heart and a bidirectional shunt at the atrial level. The other 2 cases had ventricular septal defects; in I of the latter, bilateral Blalock-Taussig aorticopulmonary shunts for treatment of tetralogy of Fallot were complicated by severe pulmonary hypertension.3 It would appear, therefore, that calcification of the pulmonary artery in congenital heart disease is not limited to patients who have had reversal of blood flow through a patent ductus arteriosus, but rather occurs in the broader group of patients with pulmonary hypertension, increased pulmonary resistance, and re-

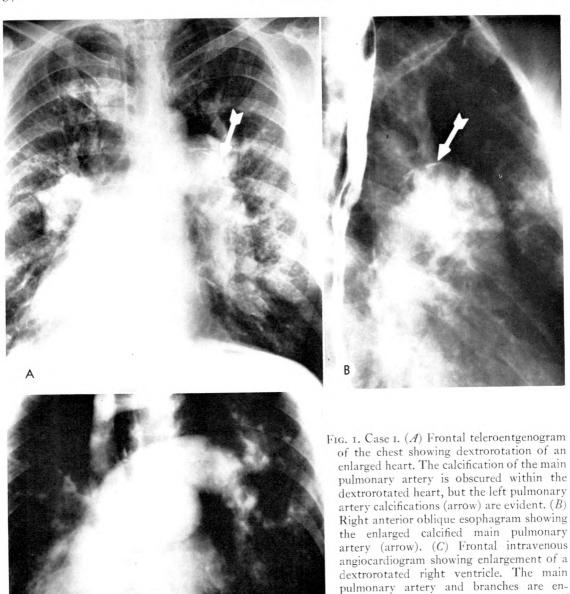
versed shunts—called by Wood, the Eisenmenger syndrome. High on the list of the causes of Eisenmenger syndrome is patent ductus arteriosus with reversal of blood flow.

REPORT OF CASES

CASE I. Calcification of an enlarged pulmonary artery, dextrorotation of the heart, and bidirectional flow through an atrial septal defect. A 69 year old Caucasian man was admitted to The New York Hospital on October 5, 1962, with a complaint of a sore tongue. Eight months earlier, at another hospital, he had had resection of the right tonsil for squamous cell carcinoma. On admission to this hospital, a tender, 1.5 cm. in diameter, mass on the right side of the tongue was found; biopsy established the diagnosis of epidermoid carcinoma of the tongue. Radiation therapy with cobalt 60, 6,400 r, was delivered to the opposing lateral parts of the base of the tongue during a 46 day period.

A routine roentgenogram of the chest on October 16, 1962, showed a dextrorotated and enlarged right heart, a calcified main pulmonary artery and left branch, and increased central pulmonary vasculature (Fig. 1, A and B). Biplane simultaneous angiocardiograms, on November 26, 1962, in frontal and lateral views, showed an enlarged dextrorotated right atrium and ventricle. The pulmonary artery and branches were also markedly enlarged. A rightto-left shunt at the atrial level with reopacification at the right cardiac structures was present at the time of the left heart filling (Fig. 1C). The great vessels were also dextrorotated.4 The electrocardiogram showed normal

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rhythm, right ventricular hypertrophy, and interventricular block. The hematocrit was 49 per cent.

The patient was readmitted twice during the next year for recurrence of carcinoma of the tongue and was treated by implantation of radium needles in the vicinity of the recurrent disease. It was estimated that the radium dosage varied between 4,400 to 7,200 r. On a visit

to the cardiac clinic on February 20, 1963, he complained of dyspnea, palpitation, and three pillow orthopnea. The electrocardiogram showed atrial flutter, rate 140, with 2:1 block. Accordingly, he was referred into the hospital.

indicates a right-to-left shunt.

larged and dextrorotated. Opacification of the centrally placed left atrium (arrow)

He gave a history that during World War I, while in the Italian navy, his heart was found to be located in the right side of the chest. He was well and without dyspnea until the time of the present admission. The apex impulse was palpated in the right midclavicular line and a systolic, ejection type (Grade 3 to 6) murmur was heard in the third to fifth interspace along the right sternal border. S2 was fixed and split. The blood pressure was 110/70 mm. Hg.

Electrical conversion on February 22, 1963, was successful and resulted in regular sinus rhythm at the rate of 75 per minute. The interventricular block, however, continued; digitalis was prescribed. At cardiac catheterization on February 26, 1963 (by Dr. Daniel S. Lukas), the catheter was advanced from the right atrium through an atrial septal defect into the left atrium and across the mitral valve into the left ventricle. It was not possible, because of the dextrorotation of the heart, to maneuver the catheter into the right ventricle or pulmonary artery. Pulmonary artery pressures, therefore, could not be obtained. A bidirectional shunt at the atrial level (left-right, 1.96 L./min. and right-left, 0.75 L./min.) was established by blood oxygen and ascorbate dilution determinations. The right ventricular pressure was 90/9; the left 130/16 mm. Hg. The patient was discharged on March 1, 1963. He was readmitted 3 more times during 1963 for recurrence of tonsillar cancer, and finally died at home on January 18, 1964, presumably of the cancer. An autopsy was not performed.

CASE II. Cyanotic congenital heart disease, calcified huge pulmonary artery, bidirectional ventricular septal defect, and right ventricular hypertrophy. A 50 year old Caucasian man was admitted to The New York Hospital on October 10, 1963, with a complaint of dyspnea on exertion. At the age of 6 years, he began to be dyspneic on exertion and "blue" when exposed to cold weather. At the age of 17 years, he had hemoptysis while running. At 27 years of age, he was rejected for military service because of a heart murmur. During the next few years he had had recurrent bouts of hemoptyses. At the age of 45 years, following a severe respiratory infection, he became markedly dyspneic, had ankle edema, and hypertension. In March, 1962, he was found unconscious in the bathroom and was rushed to a hospital where he remained in coma for 72 hours. He had an elevated hematocrit and was bled. He improved after a month. He was readmitted to another hospital in August and December of 1962 because of severe pain in the right lower

chest and dizziness. Pulmonary infarction had been diagnosed in August, and congestive heart failure in December, 1962.

On physical examination, the patient was well nourished, plethoric, and cyanotic. The fingers, toes, lips, and mucous membranes were cyanotic. The neck veins were distended and the heart was enlarged. The second sound was loud and split. A systolic ejection murmur (Grade 2-4) and a diastolic decrescendo murmur (Grade 2-4) were heard in the left third interspace and radiated along the left border of the sternum. The blood pressure was 176/104 mm. Hg. The fingers and toes were markedly clubbed. The electrocardiogram showed normal sinus rhythm, rate 80, and right ventricular hypertrophy. The hematocrit was 66 per cent. Conventional roentgenography of the heart showed calcification of the pulmonary artery, enlargement of the heart, especially of the right ventricle, and congestion of the lungs (Fig. 2, A and B). Biplane simultaneous angiocardiograms in frontal and lateral views on October 10, 1963, showed enlargement of the superior vena cava, right atrium, and ventricle. The pulmonary artery was huge, the pulmonary cusps were thickened, and there was early opacification of the left ventricle soon after visualization of the right ventricle, with faint opacification of the ascending aorta, indicative of right-to-left shunting at the ventricular levels (Fig. 2, C and D). Percutaneous transfemoral aortograms on October 10, 1963, showed intact renal arteries without stenosis; the pyelographic studies showed pyelonephritis.

The patient had 1,500 ml. of blood removed during the first 48 hours and improved. The venous pressure was not elevated. Albumin was found in the urine. He was discharged after 13 days and has been seen periodically since then in the clinic—the last visit was on April 27, 1964.

CASE III. Tetralogy of Fallot, calcification of the pulmonary artery, partial thrombosis of the left pulmonary artery, right ventricular enlargement, and pulmonary hypertension following bilateral Blalock-Taussig shunts. A 25 year old Caucasian man was studied at Flower Fifth Avenue Hospital. (Reported through the courtesy of Dr. Adele R. Altman.) He gave a history of having been admitted to Johns Hopkins Hospital where left, and later right-sided subclavian-pulmonary shunts were

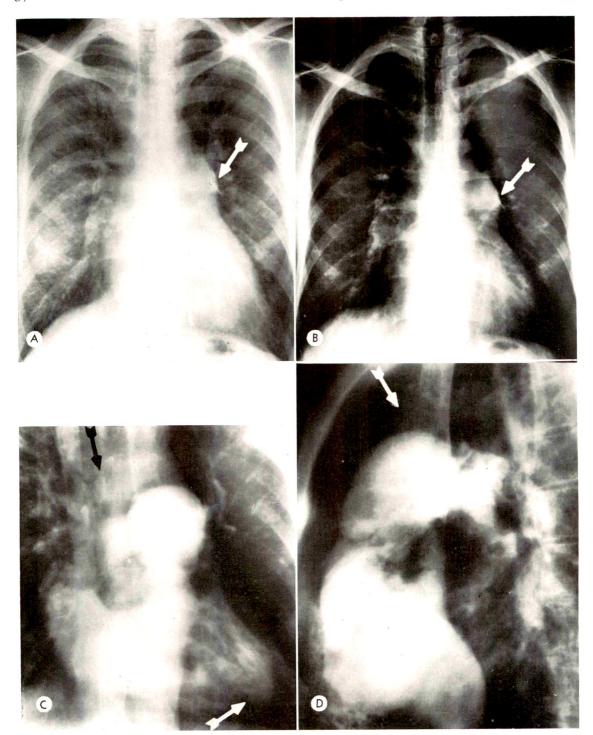


Fig. 2. Case II. (A) Frontal teleroentgenogram of the chest showing enlargement of the heart and pulmonary artery. Note calcification of the pulmonary artery (arrow). (B) Overpenetrated frontal roentgenogram of the chest showing the pulmonary arterial calcification to advantage (arrow). (C) Frontal intravenous angiocardiogram showing the enlarged right atrium, ventricles, and pulmonary artery. There is faint opacification of the left ventricle (white arrow) and ascending aorta (black arrow). (D) Lateral angiocardiogram (biplane of C) also shows the enlarged pulmonary artery and left branch. Note the large thrombus occupying the outer lower half of the left pulmonary artery (arrow).

created. Reports from that hospital verified the history of cyanosis after exercise and a cardiac murmur, beginning at the age of 2 years. Polycythemia was present at the age of 7 years. At the age of 13 years, in 1950, the hematocrit was 76 per cent and because of disabling dyspnea, a left-sided subclavian-to-pulmonary artery shunt was created. The patient improved remarkably, the hematocrit decreased to 56 per cent, and he was able to walk 3 miles without dyspnea. Five years later (1955), he again became cyanotic, the hematocrit rose to 77 per cent, and the machinery murmur was no longer heard. A right-sided subclavian-to-pulmonary shunt was made, resulting in a good continuous right-sided murmur at the base of the heart. He again improved and was able to play baseball without dyspnea. However, by 1956, dilatation of the pulmonary artery and a persistent cough developed. In 1958, the hematocrit increased and during a period of 21 days he was treated by removal of 2,800 ml. of blood. His condition worsened and in March 1959, he collapsed at work. Some improvement followed

several phlebotomies, but by 1962 the cyanosis and dyspnea were so severe that he was unable to walk.

At the time of admission, in 1962, there was marked cyanosis of the lips, tongue, mucous membranes, fingers, and toes. The fingers and toes were also clubbed. A systolic (Grade 2 to 3) murmur was heard over the precordium and radiated to the third left intercostal space along the left sternal border. No diastolic murmurs were heard. The blood pressure readings were: right arm, 90 systolic; left arm, 80 systolic; and right leg 150/80 mm. Hg. The electrocardiogram showed high P waves and right ventricular hypertrophy. The hematocrit was 58 per cent.

The roentgenogram of the chest showed enlargement of the heart and calcified main and left pulmonary arteries (Fig. 3A). On June 28, 1962, right heart catheterization and selective right ventricular angiocardiography revealed pulmonary hypertension (115/80) and right ventricular hypertension (125/12 mm. Hg). The main pulmonary artery was markedly en-

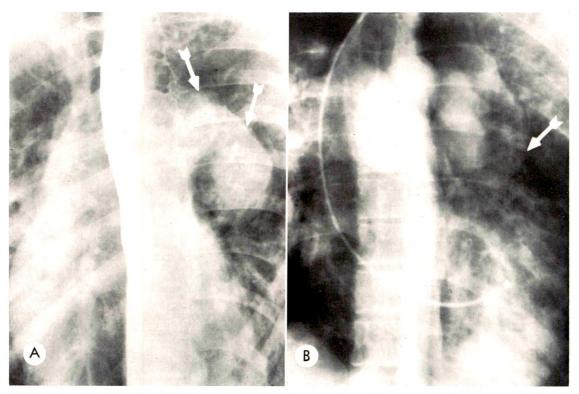


Fig. 3. Case III. (A) Frontal oblique esophagram showing the calcified main pulmonary artery (upper arrow) and left pulmonary artery (lower arrow). (B) Selective right ventricular angiocardiogram showing catheter in right ventricle. There is opacification of the pulmonary arteries and of the descending aorta. Arrow points to calcified left pulmonary artery with thrombus occupying one-half of its lumen.

larged and the left pulmonary artery contained thrombus (Fig. 3B). Following these studies he was discharged; reconstructive surgery appeared contraindicated because of the severe pulmonary hypertension.⁸

DISCUSSION

Calcification of the main pulmonary artery was evident in all of the 3 cases described above (Fig. 1, A and B; 2, A and B; and 3A). Extension of the calcification into the wall of the left pulmonary artery also occurred in 2 patients (Fig. 1A and 3A). Confinement of the calcifications to these sites was in marked contrast to that of the patients with pulmonary calcifications due to reversed blood flow through a patent ductus arteriosus.8 In the latter, additional calcifications were present in the ductus and at the aortic knob (Fig. 4, A and B; and 5, A and B). The aortic calcifications in these instances are apparently "jet plaques" commonly seen in adult patients with uncomplicated patent ducti arteriosi.6

Intravenous angiocardiography clearly established the diagnosis of reversal of blood flow through a patent ductus in a case recently published (Fig. 4, C and D).8 In Case 1, angiocardiography showed the bidirectional shunt of blood flow. However, it was necessary to perform cardiac catheterization to establish with certainty that the shunt was at the atrial level. In Case II, the clinical findings of cyanosis, clubbing of the fingers and toes, elevated hematocrit, recurrent hemoptyses, and pulmonary and cerebral emboli were characteristic of the Eisenmenger syndrome.9 Intravenous angiocardiography showed a bidirectional shunt at the ventricular level (Fig. 2, C and D). These, when assessed with the murmurs found on physical examination, were sufficient to establish the diagnosis of pulmonary hypertension and increased pulmonary resistance with reversal of shunt through a ventricular septal defect. Cardiac catheterization, therefore, was not necessary to verify the diagnosis of the Eisenmenger syndrome. In Case III, pulmonary hypertension was determined by cardiac catheterization; the right ventricular pressure nearly approached the level of the systemic pressure. This case is apparently the twelfth reported patient with pulmonary hypertension complicating the creation of bilateral aorticopulmonary shunts for treatment of tetralogy of Fallot.³

Wood, in the Croonian lecture of 1958, defined the Eisenmenger syndrome as pulmonary hypertension due to a high pulmonary vascular resistance with reversed bidirectional shunts at aortopulmonary, ventricular, or atrial levels. The cases of pulmonary calcification and reversal of blood flow through a patent ductus, recently reported,8 fit into this category. Because of dextrorotation of the heart in Case 1, the pulmonary artery could not be entered and the pressure could not be determined or the pulmonary arterial resistance calculated. The greater left to right shunt, the increased hematocrit, and large pulmonary arteries were, however, indicative of pulmonary hypertension. In this patient, death was due to cancer, rather than to heart failure. In Case II, although cardiac catheterization was not performed, the clinical, laboratory, and angiocardiographic features were sufficient to establish the diagnosis of pulmonary hypertension and increased pulmonary resistance. In Case III, selective right ventricular angiocardiography and pressure determinations provided overwhelming evidence of pulmonary hypertension and increased pulmonary resistance. Indeed, because of these data, reconstructive cardiac surgery was considered to be contraindicated.8 Finally, the previously reported cases of calcification of the pulmonary artery due to reversal of blood flow through a patent ductus arteriosus (Fig. 4, A-D; and 5, A and B) fitted into Wood's classification of the Eisenmenger syndrome.9

Not all patients with reversed aorticopulmonary or cardiac septal shunts, pulmonary hypertension, and increased pulmonary resistance have calcification of the pulmonary artery. Only 2 of 4 adult

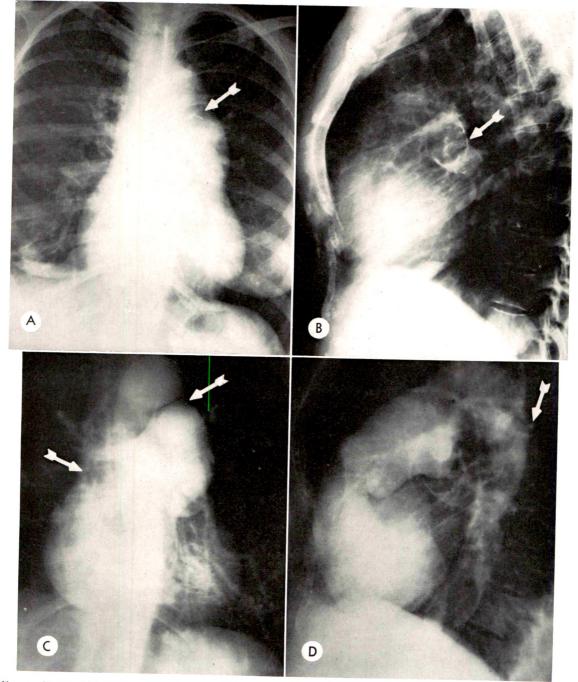


Fig. 4. Reversed blood flow through a patent ductus arteriosus in a 47 year old woman with calcification of the pulmonary artery. (A) Frontal teleroentgenogram of the chest showing enlargement of the heart and pulmonary artery. The pulmonary artery is calcified (arrow). There is a plaque in the aortic knob and another between the aorta and pulmonary artery at the site of the patent ductus. (B) Lateral roentgenogram showing cross-sectional calcification of the left pulmonary artery (arrow). (C) Frontal intravenous angiocardiogram showing opacification of the descending aorta through a patent ductus arteriosus (left-sided arrow). Arrow on the right points to thrombus occupying over half of the diameter of the right pulmonary artery. (D) Lateral angiocardiogram shows the huge pulmonary artery with opacification of the descending aorta (arrow), via a patent ductus arteriosus. (Reproduced with permission of the Am. J. Med.⁸)

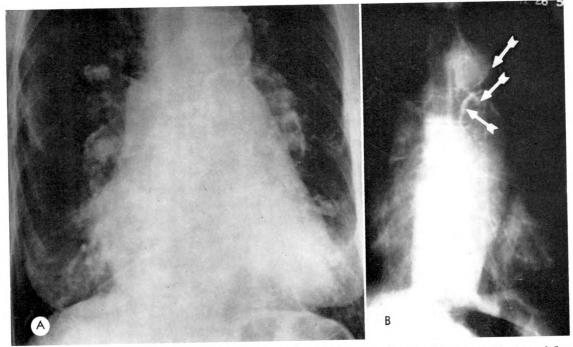


Fig. 5. Calcification of the pulmonary artery, ductus, and aortic knob in a 65 year old woman with reversed flow through a patent ductus arteriosus and left ventricular septal defect. (A) Frontal teleroentgenogram showing the enlarged heart, pulmonary artery, and plethoric lungs. (B) Overpenetrated frontal roentgenogram of the chest shows to advantage the calcification of the aortic knob (upper arrow), and pulmonary artery (lower arrows). (Reproduced with permission of the Am. J. Med.⁸)

patients with reversed ducti seen at this center since publication of the paper of Timpanelli and Steinberg⁸ in 1961 had calcification of the pulmonary artery. Of the 6 cases of reversal of blood flow in patients with patent ducti described by Dailey and colleagues,1 only 2 had calcification of the pulmonary artery. These authors found only 8 instances of pulmonary artery calcification among the 31 cases that they reviewed in the literature. Shapiro and co-authors⁵ illustrated several patients with calcification of the pulmonary artery, pulmonary hypertension, and patent ductus arteriosus in their book on cardiac calcifications, but failed to mention in which cases blood flow was reversed. Wood9 found only I case of calcification of the ductus or of the great vessels at the junctions of the duct in his large series of cases of Eisenmenger syndrome. However, the true incidence of calcification of the pulmonary artery and reversed aortopul-

monary or cardiac septal shunts will remain unknown until more attention is paid to the significance of this sign.

In the differential diagnosis, calcifications at the root of the aorta due to syphilis may be mistaken for pulmonary arterial calcifications. Syphilitic aortitis and aneurysms, especially of the aortic sinus (of Valsalva) adjacent to the pulmonary artery may, however, be clearly differentiated by angiocardiography. Usually, in syphilitic aneurysms the pulmonary artery is not enlarged. Rarely, however, cor pulmonale may follow healing and calcification of a ruptured aortic sinus (of Valsalva) aneurysm.⁴

SUMMARY AND CONCLUSIONS

Three adult men with calcification of the main pulmonary artery, the left branch, and with right ventricular enlargement were found to have congenital heart disease (pulmonary hypertension and bidirectional or reversed aorticopulmonary or cardiac septal shunts). In I patient, the shunt was at the atrial level, in another it was at the ventricular level, and in the last it followed bilateral Blalock-Taussig anastomoses for treatment of tetralogy of Fallot. The pulmonary arterial calcification was in striking contrast to the cases which had been previously reported of pulmonary artery calcifications due to reversal of blood flow through a patent ductus arteriosus. In the latter patients calcifications of the ductus and of the aortic knob ("jet plaque") at the site of the ductus were also present.

Calcification of an enlarged pulmonary artery in a patient with enlargement of the right ventricle should alert the radiologist to the possibility of congenital heart disease with reversal of blood flow, either at the aortopulmonary or cardiac septal level. Additional calcifications in the region of the ductus at the left hilus between the pulmonary artery and aorta and at the aortic knob ("jet plaque") is good evidence of reversal of blood flow of a patent ductus arteriosus. Cyanosis of the lower extremities and toes, especially after exercise, is confirmatory. Oxygen unsaturation of the lower limbs compared to the upper extremities, and, of course, angiocardiography, are confirmatory.

Cyanotic plethoric patients with enlarged right hearts and enlarged calcified pulmonary arteries should be suspected of having the Eisenmenger syndrome, *i.e.*, pulmonary hypertension and increased pulmonary resistance due to reversed cardiac or aorticopulmonary shunts. Deter-

mination of the level of the shunt in such cases may sometimes be difficult and require hemodynamic as well as angiographic studies.

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TOTAL ANOMALOUS PULMONARY VENOUS DRAINAGE INTO THE AZYGOS VEIN*

By C. A. F. MOËS, M.D., R. S. FOWLER, M.D., and G. A. TRUSLER, M.D. TORONTO, ONTARIO

TOTAL anomalous pulmonary venous drainage, though not a common anomaly, has been discussed quite extensively in the literature. A classification based on the site of attachment of the venous return at the supracardiac, cardiac, infracardiac and mixed levels has been proposed by Darling and co-workers. Total anomalous pulmonary venous return into the azygos vein would appear to be a rather rare anomaly. Four cases of this unusual malformation have been encountered recently at the Hospital for Sick Children, Toronto, with differing clinical features.

REPORT OF CASES

CASE I. H.A., a white female, delivered after a full-term pregnancy, exhibited slight cyanosis which required resuscitation, but was then well until 5 months of age, when she developed fever, cyanosis and dyspnea. At a local hospital a diagnosis of pneumonia, cardiac failure and congenital heart disease was made and treatment with antibiotics, digitalis and diuretics was carried out. After 2 months she was transferred to the Hospital for Sick Children because of persistent failure.

On admission, mild cyanosis was present at rest which increased with crying. The respiratory rate was 60 per minute and the lungs were clear to auscultation. A moderately loud blowing ejection systolic murmur was present along the upper left sternal border and a very loud rumbling mid-diastolic murmur was noted along the left lower sternal border. The first heart sound was very loud and the second heart sound was widely split with an accentuated pulmonary component. The liver was palpable 3 cm. below the right costal margin.

An electrocardiogram showed right ventricular and right atrial hypertrophy.

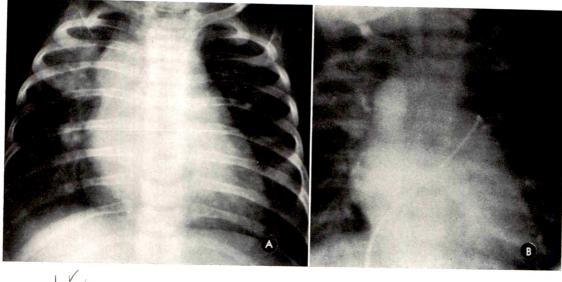
A chest roentgenogram showed cardiac enlargement with a cardiothoracic ratio of 59 per cent. The right ventricle was dilated, the main pulmonary artery prominent and there was pulmonary plethora. An oval density, 2 cm. in length by 1\frac{3}{2} cm. in width, was present in the right tracheobronchial angle. A density with a sharply defined lateral margin was seen posterior to the right heart margin and extending 2 cm. to the right of the spinal margin at its widest point. Inferiorly, the lateral margin curved medially to meet the spine at the level of the cardiophrenic angle (Fig. 1A).

Cardiac catheterization was performed and during the procedure no pulmonary veins could be probed from the left atrium. A bidirectional shunt was present at the atrial level with an over-all pulmonary to systemic flow ratio of 2:1. The femoral artery oxygen saturation was 76 per cent with a pressure of 98/57 (mean 69), while the main pulmonary artery pressure was 37/14 (mean 24) and the systemic to pulmonary resistance ratio was 6:1. The mean pulmonary artery wedge pressure was 11.

Selective angiocardiography was carried out, injecting a total of 12 cc. of sodium and methylglucamine diatrizoates (69 per cent) into the main pulmonary artery. The pulmonary trunk and its branches were slightly dilated. The contrast material from the pulmonary veins collected into a venous pool in the midline posterior to the heart and from this a dilated venous channel passed to the right and superiorly to drain into what was thought to represent a dilated azygos vein (Fig. 1B). There was subsequent filling of a dilated superior vena cava and right atrium. From the right atrium, contrast material passed into the left atrium, which appeared small. It was concluded that there was total anomalous pulmonary venous drainage into the azygos vein and an interatrial communication.

At $8\frac{1}{2}$ months of age operative correction was attempted with cardiopulmonary bypass, because of persistent cardiac failure. The 4 pulmonary veins joined to form a common venous pool from which a large vein ran to the right

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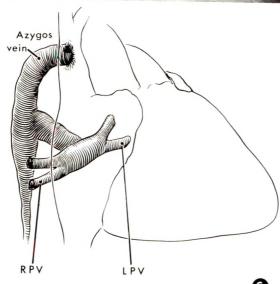


Fig. 1. Case 1. (A) Anteroposterior roent-genogram of chest showing cardiomegaly and pulmonary plethora. The density in the right tracheobronchial angle and that to the right of the spine represent the dilated azygos vein. (B) Angiocardiogram outlining the right and left pulmonary veins and common venous pool which is draining into a dilated azygos vein. (C) Diagram illustrating route taken in pulmonary venous return to the superior vena cava. RPV=right pulmonary vein; LPV=left pulmonary vein.

and slightly posteriorly to join a dilated azygos vein (Fig. 1C). On opening the large right atrium, a small patent foramen ovale, 6 mm. in diameter, was found. After excising the atrial septum, an incision was made in the posterior aspect of the right atrium, and carried across the line of the atrial septum well to the left. A similar incision was made in the common venous pool and the right superior pulmonary vein to create an anastomosis 2 cm. in length. A patch of knitted teflon was used to re-create the atrial septum. Posteriorly, this patch was sutured to the right of the original atrial septal plane and anastomosis to increase left atrial volume. The lumen of the azygos vein was nar-

rowed to a 5 mm. diameter with no apparent hemodynamic effect.

Immediately after surgery, the infant's condition appeared excellent. However, 4 hours later respiration became rapid and labored. Despite intubation and positive pressure respiration, death ensued 15 hours following operation.

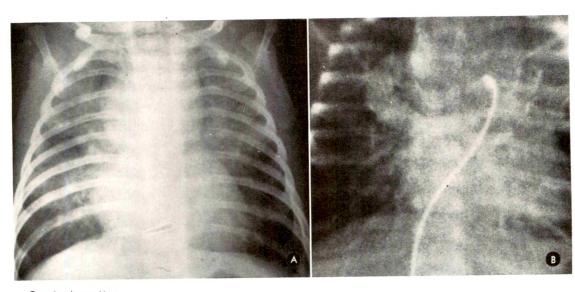
Case II. N.P., a 2 month old male infant, delivered after a normal full-term pregnancy, was well until 3 days of age, when he developed dyspnea. At 5 weeks he developed pharyngitis and mild cyanosis with crying and was admitted to the Hospital for Sick Children. On examination, he was moderately dyspneic and cyanosed

during crying. A moderate right ventricular heave was present and on auscultation there was a blowing ejection systolic murmur along the lower left sternal border with an accentuated second heart sound. A few fine inspiratory rales were heard over the chest. The liver was palpable 3 cm. below the right costal margin. An electrocardiogram showed right atrial and right ventricular hypertrophy. A chest roentgenogram revealed the cardiothoracic ratio to be 52 per cent with right ventricular enlargement. The right superior mediastinum was widened due to an oval density suggesting a dilated azygos vein, a distended superior vena cava or thymus gland. The pulmonary venous pattern was accentuated and parenchymal edema was present centrally (Fig. 2A).

At cardiac catheterization, the average oxy-

gen saturation in the venous and arterial chambers and the pulmonary and femoral arteries was similar, ranging from 62 to 67 per cent. The saturation in the superior vena cava was 70 per cent, representing an increase of 10 per cent between it and the innominate vein, while there was a rise of 21 per cent between the inferior vena cava and right atrium. The femoral artery pressure was 100/59 (mean 73) and the pulmonary artery pressure was 101/48 (mean 66), with a mean left pulmonary artery wedge pressure of 20. The pulmonary flow was less than systemic and the pulmonary resistance was greater.

Selective angiocardiography was performed, injecting a total of 9 cc. of sodium and methylglucamine diatrizoates (75 per cent) into the main pulmonary artery. The pulmonary trunk



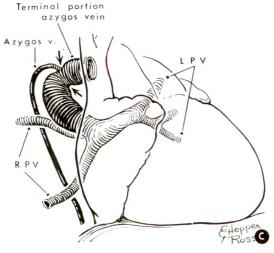


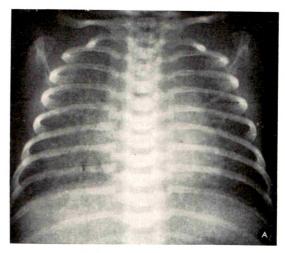
Fig. 2. Case II. (A) Plain roentgenogram showing mild cardiomegaly with moderate pulmonary edema. The oval density in the right superior mediastinum is caused by the dilated vein draining the lungs and the terminal portion of the azygos arch. (B) Angiocardiogram outlining the pulmonary veins, venous pool and dilated channel which is draining into the arch of the azygos vein. Mild narrowing is noted at the junction between the venous channel and azygos vein. (C) Diagram of angiocardiogram. The narrowing between the venous channel and azygos vein is indicated by arrows.

and main branches were dilated slightly. The pulmonary veins from both lungs were prominent and drained into a common pool, situated just inferior to the right main pulmonary artery and posterior to the heart. From this, contrast material flowed in an arching channel which passed superiorly and to the right and then medially to drain into the superior vena cava at the level of the arch of the azygos vein (Fig. 2B). The superior vena cava, right atrium and ventricle became opacified. The aorta was faintly outlined, indicating a right to left shunt, thought to be at atrial level. It was concluded that the channel was draining either into the arch of the azygos vein or directly into the superior vena cava and that there was some obstruction to the anomalous vein near its site of attachment with either of these structures. accounting for the prominence of the pulmonary veins.

Correction was attempted with cardiopulmonary bypass. The common venous pool was anastomosed to the posterior wall of the left atrium. An atrial septal defect measuring 10 mm. in diameter was closed with a pericardial patch. The ductus arteriosus was dissected and ligated, though it appeared to be closed. Postoperatively, the patient appeared well for the first 12 hours, but then developed unexplained cardiac arrest.

At necropsy, the veins from both lungs drained into a common pool situated behind the heart. From this a common channel arched upward and to the right to empty into the azygos vein, just adjacent to its junction with the superior vena cava. The portion of the azygos vein adjacent to the superior vena cava was moderately dilated, while at the junction between the common channel and the azygos vein there was slight narrowing with mild obstruction (Fig. 2C). The left atrium and ventricle were small.

Case III. Baby girl P., the result of a full-term pregnancy, was admitted to the Hospital for Sick Children at 7 hours of age in severe respiratory distress with a history of cyanosis since birth. On examination, the apex rate was 90 per minute with a normally split second heart sound and no murmur. The respiratory rate was 70 per minute and there was slight subcostal indrawing. Breath sounds were decreased bilaterally and no rhonchi or rales were heard. The liver was palpable 4 cm. below the costal margin. An electrocardiogram was nor-



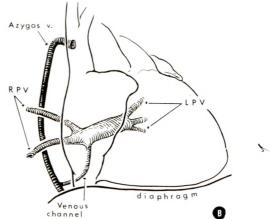


FIG. 3. Case III. (A) Anteroposterior chest roentgenogram demonstrating moderately severe pulmonary congestion without cardiac enlargement. (B) Diagram outlining the anomalous route of pulmonary drainage. The narrowed channel passing from the small common venous pool to the azygos vein is seen above the diaphragm.

mal, except for some nonspecific flattening of the T-waves. Arterial blood chemistry revealed a total CO₂ content of 11.8 mEq./L and pH of 7.22, indicating severe metabolic and respiratory acidosis. A chest roentgenogram showed moderately severe pulmonary venous congestion and parenchymal edema, without cardiac enlargement (Fig. 3A).

The child was ventilated with a Bird respirator and was digitalized, however, the cyanosis did not improve with 100 per cent oxygen. Despite correction of the acidosis with intravenous 5 per cent NaHCO₃ in 10 per cent dextrose and water and continuous ventilation, the child died 11 hours after admission.

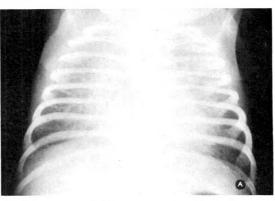
At autopsy, all 4 pulmonary veins drained into a small venous pool, situated behind the heart and from this a narrow channel passed above the diaphragm posteriorly to join the azygos vein, which lay just posterior to the descending aorta (Fig. 3B). A large ductus arteriosus was present, which at its junction with the aorta narrowed to a circumference of 5 mm. and appeared to be closing. The left atrium was small with no pulmonary venous openings. The foramen ovale was probe-patent and there was no ventricular septal defect. No coronary sinus could be identified. The lungs were heavy and relatively airless. Squamous cells and granular debris were present in some of the alveoli and there was an accompanying polymorphonuclear infiltration. The appearance was that of meconium aspiration and pneumonitis. There was extensive atelectasis and pulmonary congestion. There was no evidence of hyaline membrane disease.

CASE IV. M.B., an 8 day old female infant, delivered after a normal full-term pregnancy, was normal at birth, though slight cyanosis with crying and mild dyspnea were noted soon afterwards. Investigation at another hospital suggested a diagnosis of congenital heart disease and the infant was transferred to the Hospital for Sick Children. On admission, there was mild cyanosis at rest, which increased with crying. The respiratory rate was 60 per minute. No murmurs were present and the pulmonary second sound was normal. The chest was clear on auscultation. The liver was palpable 2 cm. below the right costal margin. An electrocardiogram showed sinus tachycardia with marked right ventricular overloading. A chest roentgenogram showed pulmonary venous congestion of moderate severity. The heart was not enlarged (Fig. 4A).

The infant was digitalized but the failure and cyanosis became more severe. At cardiac catheterization, an increase in oxygen saturation of 18 per cent was demonstrated between the high and low superior vena cava. A vessel with an oxygen saturation of 87 per cent was entered from the superior vena cava and was thought to represent either a pulmonary vein or the azygos vein. The pulmonary artery pressure was systemic and a pulmonary artery wedge pressure could not be obtained. The descending aorta was entered through a patent ductus arteriosus. The oxygen saturation here was 69 per cent, being identical to that in the right ventricle and

pulmonary artery. The pulmonary and systemic blood flows were estimated to be approximately equal and the total pulmonary resistance was equal to the systemic resistance.

Selective angiocardiography was carried out, injecting 8 cc. of sodium and methylglucamine diatrizoates (75 per cent) into the main pulmonary artery. The pulmonary trunk and its branches were slightly dilated. The contrast material from the pulmonary veins collected into a small pool posterior to the heart and to the left of the spine opposite D7. From this pool, a chamber was visible which passed superiorly into the left mediastinum for a short distance and contrast material then flowed from the mid-portion of this chamber to the right and superiorly behind the heart to enter the superior vena cava. This was interpreted as total anomalous pulmonary venous drainage into the su-



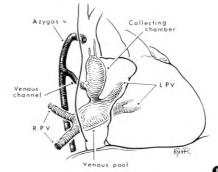


Fig. 4. Case IV. (A) Moderately severe pulmonary edema is shown without cardiomegaly in the chest roentgenogram. (B) Diagram outlining the pulmonary veins emptying into a venous pool and a dilated collecting chamber extending into the left mediastinum. Slight narrowing is noted between the pool and chamber. From the chamber a venous channel is shown passing to the right to join the azygos vein.

perior vena cava directly or into the azygos vein. The lower portion of the superior vena cava, right atrium and right ventricle were subsequently faintly opacified. The left atrium and left ventricle were not visualized. There was some delay in emptying of the contrast material from the common venous pool, thought to be due to obstruction in the venous channel prior to its termination in the superior vena cava.

At 2 weeks of age, operative correction was attempted with cardiopulmonary bypass. Initially, a patent ductus, 10 mm. in length with an external diameter of 6 mm., was identified and ligated. The common venous pool was anastomosed to a very small left atrium. On coming off cardiopulmonary bypass, the blood pressure was maintained for a few minutes, but then gradually failed and death occurred despite attempts at resuscitation.

At autopsy, all 4 pulmonary veins drained into a common venous pool situated behind the heart. This connected with a dilated venous chamber, which extended into the left mediastinum and a mild constriction as present between the pool and chamber. Several tiny veins drained the venous chamber superiorly, though drainage took place chiefly through a fairly large channel which ran behind the trachea and esophagus to join the azygos vein in the right mediastinum several centimeters below its junction with the superior vena cava (Fig. 4B). It was felt that the narrowing as well as the overall length of the venous drainage resulted in pulmonary venous obstruction. Associated cardiac anomalies consisted of a single ventricle with right ventricular morphology, a large right atrium communicating by means of a large patent foramen ovale, as well as a tiny secundum type of atrial septal defect with a small left atrium which was approximately 10 mm. in diameter. A single atrioventricular valve (tricuspid) led from the right atrium to the single ventricle with no remnant of a mitral valve. A ligated patent ductus arteriosus was present.

DISCUSSION

The literature mentions the possibility of total anomalous pulmonary venous drainage into the azygos vein, though the reported cases of this anomaly are few. Edwards⁸ in 1953 noted a case of a 10 year old girl with venous drainage into the azygos vein in association with cor biloculare

and subpulmonary stenosis. Ivemark¹¹ in 1955 (Case 12) and Kidd¹² in 1956 each reported a case of this condition occurring in male children with multiple cardiac anomalies in association with the asplenia complex. Ivemark's patient was 9 months of age, while Kidd's was 12 days at the time of death. Harris and associates, 10 in a discussion on total anomalous pulmonary venous drainage below the diaphragm, noted a male infant in whom the drainage was into the azygos vein, diagnosed by cardiac catheterization and cine-angiography. A more extensive discussion of this case is presented in a Clinical-Pathological Conference at the Children's Hospital Medical Center, Boston. Stecken and Beyer¹⁶ recently reviewed both partial and total anomalous pulmonary venous drainage into the azygos vein and added 3 cases of their own. Of the 11 cases presented, 3 were total. One reported by Miura in 1889 was a 6 month old female, and 2 female children noted by Theremin in 1884 had agenesis of the left lung with the veins from the right lung emptying into the azygos vein. Multiple anomalous pulmonary venous connections with part of the drainage into the azygos vein have also been described by Bochdalek² and Sherman.¹⁵

The normal development of the pulmonary veins in the fetus and the anomalies which may occur have been described by Edwards, 8 Neill, 13 Butler, 5 Patten, 14 Auer 1 and others. In the developing embryo, the foregut and pulmonary primordium have the same blood supply and are enmeshed in a capillary bed, the splanchnic plexus. Drainage from this plexus is into the anterior and posterior cardinal veins and the umbilico-vitelline system. Connections with the azygos system may also be present. Venous drainage from the lungs at this time is, therefore, not directly into the heart. The normal drainage of the lungs depends on the development of a common vein between the pulmonary capillary plexus and the heart. Many believe that a single evagination develops from the left atrial region and forms a connection with the pulmonary

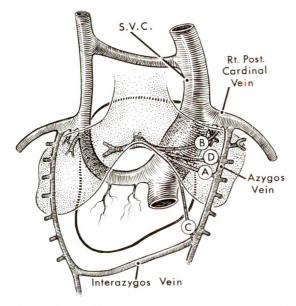


Fig. 5. Schematic diagram depicting sites of drainage into the azygos vein in the 4 cases. A represents site in Case I, B in Case II, C in Case III, and D in case IV. S. V. C.=superior vena cava. Drawing is made viewing the heart and lungs from behind. (Modified from Keith, J. D., Rowe, R. D., and Vlad, P. Heart Disease in Infancy and Childhood. The Macmillan Co.)

vessels. Duckworth⁷ is of the opinion that a single vein arises from the anterior aspect of the pulmonary plexus and extends forward into the venous mesocardium to penetrate the left atrium posteriorly just to the left of the septum primum. Whichever is the case, the earlier vascular connections disappear and the common pulmonary vein and its major tributaries become absorbed into the dorsal wall of the left atrium. Anomalies of pulmonary venous drainage may occur, according to Edwards, when there is either failure of the connection between the pulmonary plexus and the heart, or once developed, secondary obliteration takes place. Under such conditions, venous return from the lungs along one of the pre-existing pathways remains. Figure 5 illustrates the apparent routes of drainage in the 4 patients presented. The persistent connection from the lungs joined the azygos vein just above its mid-point in the thorax in Case I (A), the terminal portion of the posterior cardinal vein on the right, which becomes the

arch of the azygos vein in Case II (B), just above the dome of the diaphragm in Case III (C) and at the junction of the middle and proximal thirds in Case IV (D).

The clinical picture and course in total anomalous pulmonary venous drainage would appear to be affected by both the size of the interatrial communication and the resistance to blood flow in the pulmonary circulation. The latter is dependent to a considerable extent on the pulmonary venous pressure, which varies with the length and patency of the abnormal pulmonary vein draining the lungs.3,4 Case 1, with no obstruction to venous flow and a small patent foramen ovale, exhibited mild cyanosis, though cardiac failure was a prominent feature. Catheterization revealed an increase in pulmonary blood flow with a low pulmonary resistance. The failure in this patient would appear to be related to the small size of the patent foramen ovale and the increased volume of blood returning to the right heart, resulting in cardiac decompensation. Case II represents a situation in which moderate obstruction to venous return was present and the interatrial communication was relatively large. Cyanosis was mild, while respiratory distress was moderate. At catheterization, the pulmonary resistance was high and blood flow diminished. The increased load on the right side of the heart produced by the venous obstruction was relieved to a degree by the right to left shunt at atrial level. Case III, with marked venous obstruction, a small patent foramen ovale and a patent ductus arteriosus, presented with cyanosis from birth and severe respiratory difficulty. No catheterization was carried out, but one can conclude from the roentgenologic and pathologic findings that the pulmonary resistance would have been high and the blood flow small. Emptying of the right side of the heart would also be diminished due to the small interatrial communication. This along with myocardial anoxia apparently resulted in early cardiac decompensation and death. Case IV, with a long pulmonary venous communication, a

patent ductus arteriosus and what in effect represented a cor biloculare, showed moderate cyanosis and respiratory distress. Cardiac failure gradually became pronounced. Catheterization showed an increase in pulmonary vascular resistance and diminished pulmonary blood flow. The pulmonary venous obstruction increased systemic blood flow and myocardial anoxia caused cardiac failure.

The roentgenologic features are similarly affected by the resistance to blood flow through the pulmonary circulation, as well as the site of attachment of the anomalous pulmonary vein draining the lungs and the size of the interatrial communication. In the presence of an unobstructed pathway with increased pulmonary blood flow and low resistance, there is cardiomegaly involving the right ventricle, an enlarged pulmonary trunk and pulmonary plethora. A feature of diagnostic significance in Case 1 with these findings was the presence of a moderately well circumscribed density in the right tracheobronchial angle, which represented a dilated arch of the azygos vein. The roentgenologic features in total anomalous pulmonary venous drainage below the diaphragm are well known. Typically, the lungs show a reticular pattern due to venous congestion or a diffuse clouding resulting from parenchymal edema, and the heart in the frontal projection is usually of normal size. Cases III and IV exhibited features which were indistinguishable from this roentgenologically. Hemodynamically, obstruction to the pulmonary venous flow is present in both types of anomalous drainage, resulting in similar roentgen findings; however, the abnormal site of attachment of the pulmonary vein is subdiaphragmatic in one and supradiaphragmatic in the other. Case II, with less marked venous obstruction, showed findings which were intermediate between Case I and Cases III and IV. Mild right sided cardiac enlargement was present with venous engorgement and mild pulmonary edema centrally, resulting from pulmonary venous obstruction. A mass was present in the right tracheobronchial angle, though this was more oblong in appearance than in Case I and was subsequently proven to be due to a combination of dilated azygos arch and terminal portion of the anomalously draining pulmonary vein.

A more clear-cut diagnosis may be made by selective angiocardiography with injection of contrast material into the main pulmonary artery. This procedure was performed in 3 cases, while in the fourth, Case III, the child was too ill. In these, the pulmonary veins from both lungs were seen to collect into a common venous pool posterior to the heart with no connection to the left atrium. A venous channel was visible draining the pool, though it was not certain whether this channel emptied directly into the superior vena cava or in fact connected with the azygos vein before drainage terminated in the vena cava. The presence of an oval density in the right tracheobronchial angle on the plain roentgenogram would appear to be in favor of drainage into the azygos vein, with dilatation of this structure when no obstructive element to venous return is present, as in Case 1, or is mild, as in Case II.

The presence of more marked obstruction resulted in a chest roentgenogram indistinguishable from total pulmonary venous drainage below the diaphragm. Angiography, however, in Case IV showed venous return not to be subdiaphragmatic. Again, it was not definite whether the site of termination of the draining channel was directly into the superior vena cava or the azygos vein. No density was present in the right superior mediastinum in this instance, as the arch of the azygos vein was not dilated. The left atrium was visualized in Case I due to the presence of a right to left shunt through a patent foramen ovale and this chamber was small. The level of the shunt in Case II was not definitely outlined though was presumed to be at atrial level, while in Case IV no communication was recognized, probably due to dilution of the small amount of contrast material returning to the right side of the heart.

Operative correction of total anomalous pulmonary venous drainage into the azygos vein is completely feasible. The techniques are essentially identical to those utilized for other supracardiac variants of this anomaly. In older infants, anastomosing the left atrium to the common venous pool and closing the atrial septum are most easily accomplished by a right-sided approach. The atrial septal patch should be sutured to the right of this anastomosis in order to enlarge the left atrial chamber; otherwise, cardiac output may be restricted.¹⁷ The total correction could be completed in one stage by ligating the azygos vein, but it would appear preferable to leave it as a "safetyvalve." Regardless of the surgeon's skill, certain anatomic variables, such as the size of the left atrium and the size and position of the common venous pool, have a marked effect on the ease of operation and the prognosis. In our younger infants results in all forms of total anomalous pulmonary venous drainage have been unsatisfactory and our present feeling is that a less involved repair, utilizing a shorter period of cardiopulmonary bypass, might improve survival. Perhaps creating a moderate anastomosis between the left atrium and common venous pool with the temporary assistance of cardiopulomonary bypass would save some of these desperately ill infants.

SUMMARY

The clinical, roentgenologic, angiocardiographic and operative or postmortem features in 4 cases of total anomalous pulmonary venous drainage into the azygos vein are presented. The findings were affected by the resistance to blood flow in the pulmonary circulation and the size of the interatrial communication. In the presence of a nonobstructed venous return, there was cardiomegaly, increased pulmonary artery vascularity, mild cyanosis, moderate dyspnea, cardiac failure and hepatomegaly. When venous return was obstructed, the heart was of normal or near-normal size, pulmonary venous congestion and edema

were prominent without pulmonary plethora, cyanosis and dyspnea were more pronounced and there was cardiac failure and hepatomegaly. Death in the latter group tended to occur early.

Roentgenologically, the presence of a mass in the right tracheobronchial angle was noted in 2 cases in which venous obstruction was absent or mild. This was shown to represent a dilated azygos vein arch alone or in combination with the terminal portion of a dilated anomalous pulmonary channel draining the lungs. When the anomalous pathway was long or very narrow with resultant moderate to severe obstruction, no mass was visible on the plain roentgenogram, as the azygos vein was not distended. Selective angiography showed the anatomy of the anomalous venous return in 3 cases in which this procedure was performed and the results were correlated with the surgical or postmortem findings.

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ANGIOGRAPHIC FEATURES OF PRIMARY VENOUS OBSTRUCTION OF UPPER EXTREMITY*

PAGET-VON SCHRÖTTER SYNDROME

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HUGHES, 7 in 1949, in a classic review of 320 cases of venous obstruction of the upper extremity, called attention to the rapid onset of pain, swelling, and discoloration of the arm in an otherwise healthy person. He pointed out that these symptoms and signs constituted a syndrome and proposed that in the absence of any unanimity regarding its etiology and pathology, that it be named the Paget-Schroetter syndrome after the authors who described the first cases. 12,21 (Incidentally, Hughes anglicized von Schrötter's name to Schroetter and left out the "von." Since this causes havoc with bibliographic lists, it seems wise to retain the German.) Recently, Adams and co-authors1 suggested that the malady be called primary deep venous thrombosis of the upper extremity rather than primary thrombosis, 11 spontaneous thrombosis, 5 effort thrombosis,3,8 and traumatic thrombosis.16 These authors argued that although trauma of some type initiated the onset of symptoms in most cases, a significant number of thromboses occurred without known injury. Although it is desirable to simplify the nomenclature of disease, onset with direct or indirect trauma, the physical and contrast roentgen findings, and the clinical course of the malady are better appreciated when it is regarded as a syndrome. Because not all patients with the syndrome have venous thrombosis, 6,22 and this is true of 2 of the cases herein reported, it seems better to retain the broad title of Hughes,7 "venous obstruction of the upper extremity" (Paget-von Schrötter syndrome) rather than the designation of Adams et al.,1 "primary deep venous thrombosis of the

upper extremity." However, it seems desirable to retain the term "primary" in the nomenclature of the syndrome because it serves to emphasize the unique (primary) nature of the disease. Because angiography provides significant information regarding the site and type of the venous obstruction and collateral pathways, it is recommended for diagnosis and evaluation of the effect of therapy. These data, obtained chiefly from angiographic study of a series of II cases at this center, are herein recorded and are the reason for this report.

MATERIALS AND METHODS

A search of the medical records at The New York Hospital disclosed that II patients with primary venous obstruction of the upper extremity had been studied angiographically while in the hospital during the years 1948 to 1965. Venous obstruction of thrombosis associated with heart disease,10,19 mediastinal tumor and lymphadenopathy, cancer, or neoplasm of any type were excluded from the series. Angiography was performed by percutaneous insertion of the special 12 gauge needle stop-cock unit into a large cubital vein and injection of 30 to 50 ml. dilute organic contrast medium according to the Robb-Steinberg method.¹⁵ Early in the series, 2 films per injection, using a stereocassette changer, were obtained. Later, when serial film devices became available, multiple exposures usually at the rate of I per second were made. The circulation time was routinely determined by preliminary intravenous injection of a mixture of 3 ml. of 20 per cent solution of decholin and 15

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ml. physiologic saline solution in a 20 ml. syringe injected through the Robb-Steinberg cannula. This provided a guide for the timing of the total duration of the roentgen exposures and also accurately foretold the degree and extent of the venous obstruction. Injection of the contrast material was at first made manually. Recently, however, pressure injections of 3–5 kg./cm.² were used.¹8 Venous pressures were obtained by attaching a manometer to the Robb-Steinberg needle and reading the pressure at the level of the angle of Louis prior to angiography.

FINDINGS

In Table 1 the clinical, angiographic and pressure data of the 11 patients with venous obstruction of the upper extremity are listed. Six were men and 5 were women. The ages varied from 18 to 76 years with an average of 38 years. In 6 patients, the right upper extremity was involved, in 5 it was the left. Sudden onset of pain and/or swelling of the upper extremity occurred in all but 2 patients (82 per cent), in whom the onset was more gradual, of I and 2 years, respectively, before medical aid was sought. A history of some type of trauma was elicited in all but 3 patients. Direct trauma varied from awakening with pain after falling asleep on the arm (Case 1), having a case of whiskey falling on the shoulder (Case II), falling on arm (Case VI), and slipping while swinging a sledge hammer (Case IX). Constant use of the extremity was described by a grocery clerk (Case III), an elevator operator (Case x), and a drawing teacher (Case XI). In 3 patients, no history of trauma was elicited, but I patient (Case VIII) suffered from hyperabduction syndrome.23 Another patient (Case 1) also had a healed fracture of the clavicle on the same side as the obstruction.

Marked venous engorgement with collateral circulation of the involved arm, pectoral region, and shoulder girdle was evident in every case and was well demonstrated by infrared photography (Fig. 1B). Angiography clearly visualized the site of

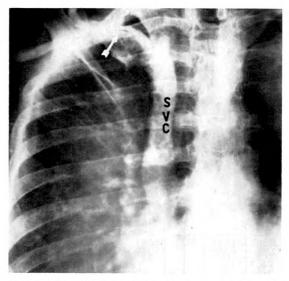


Fig. 1. (A) Case III. Angiogram showing chronic narrowing of the right subclavian vein (arrow). Note that the innominate vein and superior vena cava (SVC) are intact.

venous obstruction in every instance. In I patient the subclavian vein was only partially obstructed (Fig. 1A). In another, partial left subclavian vein obstruction was apparently due to an hypertrophied terminal axillary vein valve (Fig. 1C). Axillary vein thrombosis in an acute case is shown in Figure 1D. In a chronic, long standing patient with venous obstruction of I year's duration (Case XI), the axillary vein thrombosis was accompanied by poorly developed collateral circulation (Fig. 2A).

DISCUSSION PATHOGENESIS

Indentation (stenosis) of the subclavian vein as it passes over the first rib has been regularly observed during intravenous angiocardiography and this may be termed the physiologic point of constriction (Fig. 2B). In some patients, it may become exaggerated when the arm is elevated and seriously hamper blood flow into the thorax (Fig. 3A). This may, however, be alleviated by injecting the contrast medium with the arm extended beside and at the same level of the body in the supine position (Fig. 3B). This subclavian vein narrowing is apparently related to the close relationship of the

Table I

PRIMARY VENOUS OBSTRUCTION OF THE UPPER EXTREMITY

(PAGET-VON SCHRÖTTER SYNDROME)

					· · · · · · · · · · · · · · · · · · ·					
Case No.	New York Hospital No.		Age (yr.)	. Site	Chief Complaint Trauma Angiographic Treatme		Treatment	Venous Pressure (H2O), Remarks, and Follow-up		
I	5090406	м	55	Right subclavian vein	Awoke with swelling of right arm of 4 hours' duration	Sleeps with arm under body	5/19/48 Thrombosis of right subclavian vein	Heparin and dicumerol, discon- tinued after 10 days	Old healed fracture of right clavicle 2 months following dis- charge, alight residual swelling; no impairment of motion	
	564103	M ,	25	Right axillary vein	Pain and swelling of right arm of 12 hours' duration	Case of whiskey fell on shoulder 24 hours earlier	2/28/50 Thrombosis of right axillary vein	Dicumerol for 8 days	425 ml. Stellate ganglion block (right) Attends clinic. Arm size reduced, no disability. 14 year follow-up	
ш	528782	F	43	Right subclavian vein	Swollen right arm for 2 years	Works in grocery store, lifting cans of food all day	0bstruction of right subclavian vein (Fig. 1A)		Last seen in 1965, no com- plaints referable to arm (Similar case reported by Horwitz and Zinsser*)	
IV	681720	M	20	Right axillary vein	Right arm larger than left for 1 month	Sudden pain after lifting a heavy object 36 hours earlier	4/22/54 11/9/54 Thrombosis of right axillary vein	Tromexan for 7 months	350 ml. Found to have hyperabduction syndrome ²² Scalenotomy and excision of first 2 ribs; improved	
	717758	М	23	Left axillary vein	Left arm black and blue for 11 days		8/20/55 Left axillary vein thrombosis	Heparin and dicumerol	Gradual decrease in swelling in 8 days	
VI	740776	F	76	Left axillary vein	Pain and swelling of left arm of 12 days' duration	Fell on collapsible chair, landing on arm, 2 weeks carlier	7/23/56 Thrombosis of left axillary vein		340 ml. Infrared photograph showed prominent col- laterals left thorax (Fig. 1B) Swelling of arm gone in r month	
VII	594947.	F	20	Left subclavian vein	Swelling of left arm and shoulder for 41 months		6/18/57 Markedly hyper- trophied terminal ardiary valve with obstruction of left subclavian vein (Fig. 1C)	Dicamerol	Associated hyperabduction syndromes One year later, improved Similar case reported by Wilder et al. ²²	
vIII	801351	F	43	Leit subclavian vein	Swelling of left arm of 5 weeks' duration		8/5/58 Thrombosis of left axillary vein with many collaterals	Dicumerol	Suffered stiff neck 3 months earlier Hyperabduction syndrome also present ²⁸	
IX	907755	M	67	Right axiliary vein	Swollen right arm for 1 day	Uses a sledge hammer in work, and 3 days earlier, slipped while swinging it	5/12/64 Thrombosis of right axillary vein with marked collaterals (Fig. 1D)	Heparin and coumadin	170 ml. Swelling and pain gone 3 months later; anticoagu- lants stopped	
х	972469	M	18	Left axillary vein	Swollen and stiff left arm for 5 days	An elevator oper- ator; uses left arm to open and close doors	7/10/64 Thrombosis of left axillary vein	Warfarin for 3 months	Employee of hospital, changed job Swelling and pain disap- peared in 3 weeks Being soon regularly; last visit October 29, 1005; no complaints referable to arm	
xı	1005167	F	axillary right arm and continuou		Drawing teacher and continuously using hand and arm	a/11/65 Thrombosis of right arillary vein with few collaterals (Fig. 2A). Left subclavian vein stenosis at site of "physiologic obstruction." Left innominate vein and superior vena cava intact (Fig. 2B)		aco ml. No medication given Unchanged ro months later Continues to have pain, swelling, and impaired function of right upper extremity		

shoulder girdle structures and vein and may be better understood by reviewing the anatomic course of the subclavian vein.

The axillary vein begins by union of the brachial and basilic veins at the lower border of the teres major muscle. It then crosses anteriorly to the head of the humerus and subscapularis muscle and passes beneath the pectoralis minor muscle close to the insertion of the coracoid process. It then continues under the clavicle, where at the lateral border of the first rib, it is joined by the cephalic vein and becomes the subclavian vein. This vein is short, passes over the first rib, and proceeds anteriorly to the scalenus anticus muscle to unite with the internal jugular vein to become the innominate vein in the thorax. The subclavian vein traverses the first rib via a tract called the costoclavicular. This is in relation, anteriorly, to the clavicle, an underlying subclavius muscle, the cartilage of the first rib, and to the costocoracoid ligament. Posteriorly, the anterior scalene muscle and, inferiorly, the first rib bound the space.

Under normal conditions, the costoclavicular space is more than adequate to accommodate the brachial vessels. However, when edema and swelling follow trauma, serious impingement of the vein may occur and cause obstruction to blood



Fig. 1. (B) Case vi. Infrared photograph showing the marked venous collateral circulation of the left arm, shoulder, and thorax due to left axillary vein thrombosis. R and L are right and left sides, respectively.

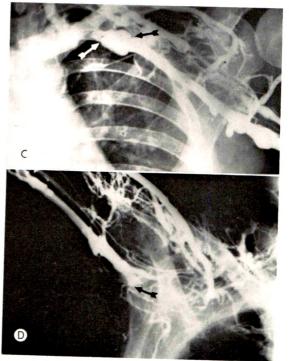


Fig. 1. (C) Case VII. Hypertrophied terminal axillary venous valve (black arrow) with narrowing of the subclavian vein (white arrow). Note the extensive collaterals between the cephalic and axillary veins. (D) Case IX. Twenty-four hours after injury, right axillary vein thrombosis (arrow) with well established collaterals.

flow and thrombosis of the vein.¹⁷ Indeed, it is precisely for these reasons that operative procedures for relief of shoulder girdle syndromes have been devised.⁹

Because of the physiologic point of narrowing of the subclavian vein, it is easy to understand why trivial trauma or persistent aggravation at this point of narrowing by constant or intermittent use of the arm may produce, first, obstruction, then reduced blood flow, and finally thrombosis. That obstruction may occur without thrombosis is demonstrated in Figure 1A. It has also been described by Horwitz and Zinsser.6 Another type of obstruction of the subclavian vein has been described by Wilder and co-workers22 and such a cause is illustrated in Figure 1C (Case VII). Once thrombosis of the subclavian vein occurs, it may affect the axillary vein retrogradely, or else progresses to involve the innominate

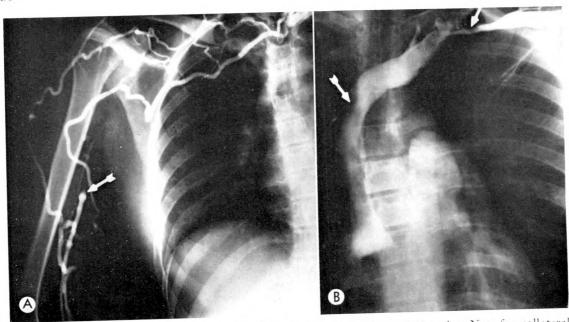


Fig. 2. Case XI. (A) Chronic right axillary vein thrombosis (arrow) of I year's duration. Note few collateral channels. (B) Left arm injection (with arm elevated) showing point of phys.ologic stenosis of the left subclavian vein (upper arrow). The left innominate vein and superior vena cava are intact. Lower arrow points to site of entrance of right innominate vein. The failure to fill the right innominate vein after long serial roentgenography (see Fig. 4D) suggested that thrombosis had extended to the site of junction of the other innominate vein.

vein. It appears, therefore, that the strategic location of the subclavian vein, with its point of physiologic narrowing, and its relationship to neighboring structures, lends itself to injury, obstruction, and thrombosis. Progression of the thrombosis leads to extension to the adjacent axillary or innominate veins.

CLINICAL FINDINGS

Clinically, the sudden onset of primary venous obstruction follows a constant, repetitive pattern. monotonous, and Trauma, direct or indirect, in a previously healthy person is followed by pain, swelling, redness, and increased venous pressure of the upper extremity. Sometimes, a tender thrombosed axillary vein can be palpated. Collateral vessels over the arm, shoulder girdle, and pectoral muscles of the involved side become evident (Fig. 1B). Anticoagulant therapy is usually effective, but the association of shoulder girdle and hyperabduction syndromes may require prophylactic surgery.9 Although pulmonary emboli

did not occur in the series of cases reported here, it is always a threat and should be constantly kept in mind.^{1-3,7,17}

ROENTGENOGRAPHIC DIAGNOSIS

Definitive diagnosis is made by venous angiography of the involved arm. Although earlier reports of the value of venous angiography in this disease have been disparaging,7 the newer dilute contrast agents, multiple serial roentgenographic devices, and rapid injection via a large bore needle have considerably enhanced the safety and worth of the procedure. Not only may the site of venous thrombosis be recognized (Fig. 1D), but other causes of venous obstruction can be differentiated. In Figure 1A, venous obstruction due to chronic undue narrowing of the right subclavian vein, similar to the case of Horwitz and Zinsser,6 is shown. In another patient, an unduly hypertrophied terminal valve of the axillary vein, very much like the case of Wilder et al.,22 was responsible for venous obstruction (Fig. 1C). Physiologic narrowing with-

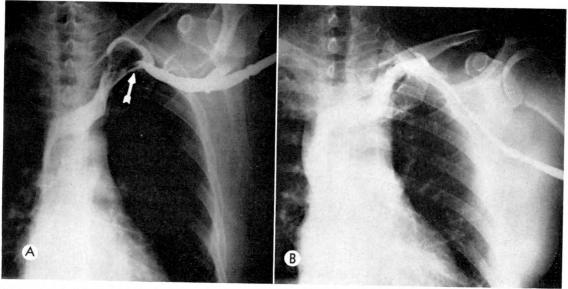


Fig. 3. (A) Left arm injection of contrast agent with arm elevated in a 46 year old patient produced marked narrowing of the subclavian vein (the physiologic point of obstruction). (B) Another injection with the arm at the side of the body alleviated the stenosis.

out serious consequences was frequently evident (Fig. 2B; 3A; and 4E). On the other hand, undue swelling of the left arm was demonstrated to be due to superior vena caval and left innominate vein narrowing in another patient (Fig. 6, A and B). The presence of right hilar masses (Fig. 4C), despite the presence of right axillary vein thrombosis (Fig. 4, A, B and C), negated against the venous thrombosis

being primary. Subsequently, this was confirmed by a positive Class v Papanicolaou sputum specimen which established pulmonary carcinoma as the cause of the right axillary vein thrombosis. Finally, angiography is capable of differentiating other types of venous thrombosis from primary thrombosis of the upper extremity. Figure 5 is an example of multiple venous thromboses of the arm in a woman with lymph-

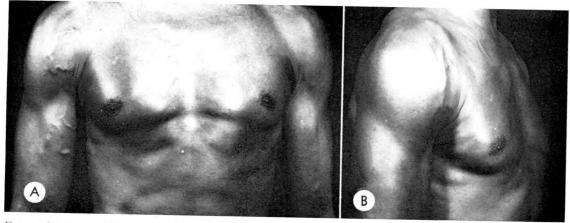


Fig. 4. Carcinoma of the lung with right axiliary venous thrombosis in a 56 year old Negro simulating primary venous thrombosis of the right arm. (A) Frontal photograph showing venous engorgement of the right arm, shoulder, and anterior thorax. (B) Lateral photograph of upper arm and thorax also showing venous engorgement.

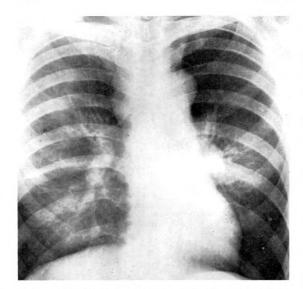


Fig. 4. (C) Frontal teleroentgenogram of the chest showing widening of the superior mediastinum and enlargement of the hilus.

edema following radical left mastectomy. While the differentiation between this and primary venous obstruction of the extremity was evident on inspection, the extensive nature of the thrombosis was detailed by angiography. Finally, prognostic data of importance for the management of a case may be secured by evaluating the efficiency of the collateral channels visualized by angiography. For instance, the sparse collateral circulation following thrombosis of the axillary vein of a year's duration is not a favorable sign (Fig. 1D) compared to the plethoric collateral circulation demonstrated in another more acute case (Fig. 1C).

SUMMARY AND CONCLUSIONS

Primary venous obstruction of the upper extremity in previously healthy individuals usually occurs after trauma. Pain, swelling, tenderness, and increased venous pressure of the upper arm, and subclavian and axillary vein thromboses frequently follow. The onset and clinical course of the malady follows a pattern named the Paget-von Schrötter syndrome, by Hughes, after the authors who described the first cases, and

this designation deserves to be perpetuated. Because anticoagulant therapy alleviates symptoms, prevents propagation of the thrombus to collateral veins, and protects against pulmonary embolization, early diagnosis and treatment are desirable. Angiography is recommended for definitive diagnosis. Other causes of venous throm-

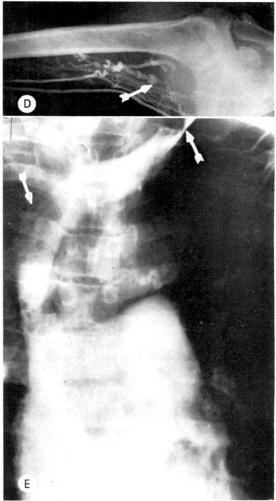


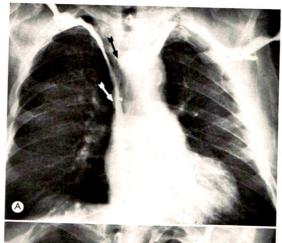
Fig. 4. (D) Venogram of the right arm showing thrombosis of the axillary vein (arrow) with collaterals of the shoulder, neck, and axilla. (E) Venogram of the left arm showing the point of subclavian stenosis (upper arrow) and intact left innominate vein and superior vena cava (lower arrow). Again, the failure to fill the right innominate vein, late in the serial study (D) suggests extension of the thrombus to the site of junction of the innominate veins.

bosis, such as intermittent subclavian vein occlusion, central great vessel occlusions, and multiple occlusions associated with lymphedema, may also be differentiated by angiography.

Angiography has also revealed a physiologic point of narrowing of the subclavian vein as it crosses the first rib. Narrowing of the coracoid space by edema following trauma, ununited fractures of the clavicle, and undue pressure by the structures adjacent to the subclavian vein lead to production of shoulder girdle syndromes and favor venous thromboses. Adjunct surgery for correction of these defects following anticoagulant therapy are, therefore, recommended in some cases. Visualization of the state of the venous collaterals may also be of prognostic significance. The sparseness of the collateral circulation in a case of axillary vein thrombosis of long standing



Fig. 5. Lymphedema following radical left mastectomy $3\frac{1}{2}$ years earlier in a 58 year old woman showing multiple stenosis of the brachial, axillary, and innominate veins (arrows). This pattern of multiple venous stenoses is strikingly different from that caused by primary venous thrombosis.



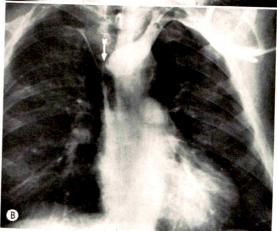


Fig. 6. Stenosis of the right and left (terminal portion) innominate veins and superior vena cava (of unknown etiology) in a 65 year old man simulating left upper arm venous obstruction. (A) Bilateral arm injection of contrast medium shows marked narrowing of the right innominate vein, superior vena cava, and terminal end of the left innominate vein (arrows). (B) Later in the series, the right innominate vein and superior vena cava were practically empty, but the left innominate vein was still dilated and opacified (arrow).

arm swelling was ominous and in marked contrast to that of an acute case with plethoric venous collaterals.

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LAMINAGRAPHIC STUDIES OF THE VASCULAR PATTERNS IN CANCER OF THE LUNG WITH SPECIAL REFERENCE TO THE "CIRCUMSCRIBED" VARIETY

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ESPITE useful information often available from able from an inspection of conventional chest roentgenograms, scant attention appears to be paid to the so-called lung markings, although they represent, in fact, a pattern of the pulmonary vessels. Indeed, if sought for, recognizable abnormalities in a variety of cardiovascular and pulmonary diseased states can be identified without enhancement by special technique. Reference is made here to identification and not to techniques so often essential for precision and diagnosis. In cancer of the lung, we have long noted vascular alteration, depending upon whether the tumor was diffuse and infiltrating, or localized.

The term "circumscribed" was introduced in 1934² and its significance emphasized to define the form of pulmonary cancer usually characterized by limited or no regional lymph node involvement and, therefore, most amenable to surgical relief. Today, these lesions as seen in the roent-genograms are termed "coin" lesions, and are usually discovered in routine roentgenograms. By way of contrast to diffuse infiltrative tumors, "circumscribed" lesions do not offer adequate features for diagnosis in conventional roentgenograms.

The abnormalities of the vascular pattern to be seen in infiltrating cancer of the lung are often great. These were set forth dramatically by the contrast angiographic studies of Dotter and Steinberg. Recent contrast studies of the bronchial arteries by Viamonte³ have demonstrated tumor vessels in bronchogenic carcinoma.

We have learned that distortion of the vascular pattern created by "circum-

scribed" tumors can be identified in conventional roentgenograms when the lesion is the size of a quarter or larger. However, only when laminagraphy is added is more precise information useful for diagnostic purposes available. Not only does laminagraphy reveal additional vessels and make possible differentiation between arteries and veins, but also identifies clearly the distortion of the vessels in immediate relationship to the lesion.

In the illustrative cases presented below, all laminagraphic sections were made with the patient supine.

ILLUSTRATIVE CASES

CASE I. C.R., a 38 year old white female had chronic rheumatoid arthritis. A conventional chest roentgenogram (Fig. I) showed no abnormalities in the heart or lungs. Figures 2, 3 and 4, laminagraphic sections at 6, 8 and 12 cm., show how much of the vascularity of the lungs becomes apparent when laminagraphy is done. Section 8 (Fig. 3) most clearly demonstrates the course of the pulmonary veins.

Case II. D.B., a 67 year old patient, presented with weakness, fatigue and cough of 6 months' duration.

A conventional chest roentgenogram (Fig. 5) on September 7, 1960 showed an ill-defined density in the right upper lobe. Laminagraphy at the 13 cm. level (Fig. 6) showed an irregular notched lesion in the right upper lung field; at the 6 cm. level (Fig. 7) a displaced vessel at the vaguely defined lesion; and at 8 cm. (Fig. 8) two elongated "taut" vessels in immediate relation to the lesion.

Pathology (83416) of the surgical specimen revealed squamous cell carcinoma of the lung.

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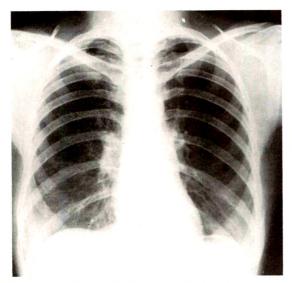


Fig. 1. Case 1. Conventional chest roentgenogram is normal.

Case III. L.S., a 72 year old patient, was admitted for vague abdominal complaints. A chest roentgenogram in March, 1959 was normal.

A conventional study (Fig. 9) on February 4, 1960 demonstrated a faint infiltrate in the right upper lung field adjacent and lateral to the hilus. A laminagram (Fig. 10) showed displacement of vessels about the lesion.

The patient was discharged and died within the year with symptoms of brain metastases.

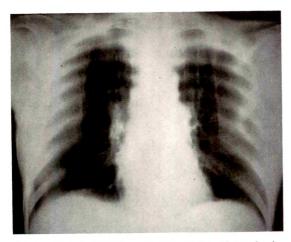


Fig. 2. Case I. Laminagraphic section through the posterior portion of the lungs shows the course and pattern of the vessels.

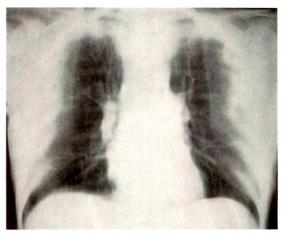


Fig. 3. Case I. Laminagraphic section through the mid-portion of the lungs clearly defines pulmonary veins in addition to the arteries. The upper lobe veins cross the hilus of each lung while the lower lobe veins pass horizontally to the left atrium.

Case IV. S.F., a 64 year old patient, presented with acute onset of pain in the back, after lifting, of I month's duration. A roentgenogram showed a collapse of LI and large lymph nodes in the right axilla.

A conventional chest roentgenogram (Fig. 11) on June 22, 1960 demonstrated a hazy infiltrate in the right upper lung above and lateral to the hilus and a curved and hooked appear-

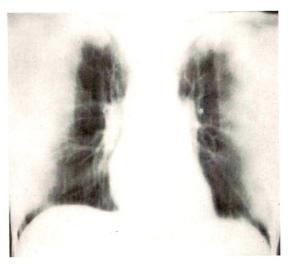


Fig. 4. Case I. Laminagraphic section is further anterior than in Figure 3. The abundant vascular shadows are quite striking when compared to the conventional study (Fig. 1).

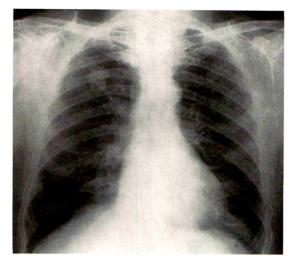


Fig. 5. Case II. An irregular density is seen in the right upper lobe on the conventional roentgenogram.



Fig. 6. Case II. Laminagraphic section shows an irregular notched lesion with few vessels at this level.



Fig. 7. Case II. Laminagraphic section 7 cm. posterior to Figure 6 shows a vessel being displaced medially by the tumor.

ance of a vessel on the medial aspect of the lesion. A laminagram at the 9 cm. level (Fig. 12) showed bizarre, distorted vessels about the lesion.

Biopsy of the axillary lymph nodes (80887) on June 27, 1960 revealed metastatic carcinoma.

Case v. M.S., a 60 year old patient, had a nonproductive cough.

A conventional chest roentgenogram (Fig. 13) on March 24, 1960 demonstrated a lobulated density in the right lower lung. A laminagram at 9 cm. (Fig. 14) showed a displaced, curved branch of the lower lobe artery laterally and an irregular "taut" vessel medially.

and an irregular "taut" vessel medially.

Pathology (78586) on April 13, 1960 of a mass 6 cm. in diameter in the right lower lobe revealed adenocarcinoma with metastatic carcinoma of the lymph nodes.

CASE VI. J.B., a 35 year old patient, had pain in the left shoulder and scapula for 2 months. He

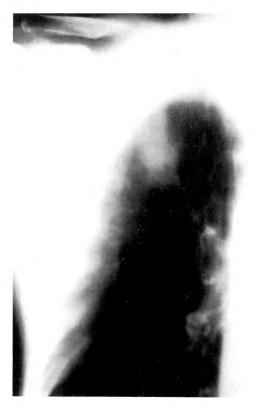


Fig. 8. Case II. Laminagraphic section 2 cm. anterior to Figure 7 shows two elongated "taut" vessels passing in relation to the upper and lower portions of the tumor.

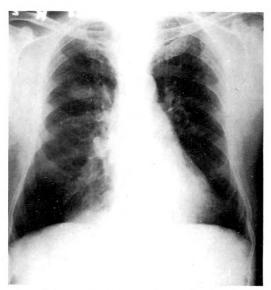


FIG. 9. Case III. An irregular density is seen in relation to the anterior portion of the third right rib on the conventional roentgenogram.

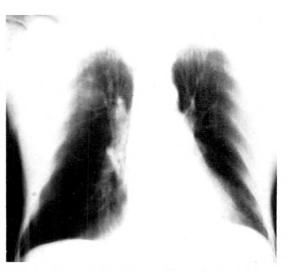


Fig. 10. Case III. Laminagraphic section shows vessel distortion and displacement by the tumor.

had had hemoptysis on several occasions for a period of 5 years. He had repeated bouts of pneumonia from 1949 to 1953.

A conventional chest roentgenogram (Fig. 15) on October 28, 1959 demonstrated a dense infiltrate in the left upper lung medially. A laminagram at 10 cm. (Fig. 16) showed a displaced curved vessel lateral to the density.

Pathology (73275) revealed that almost the



Fig. 11. Case IV. A hazy density is seen in the right upper lobe on the conventional roentgenogram. The arrow indicates a vessel medial to the lesion with an abnormal curved appearance.

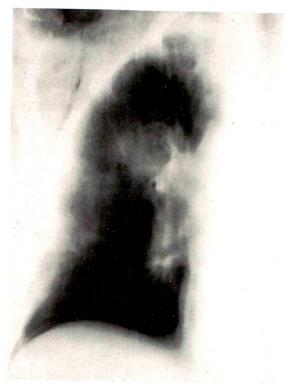


Fig. 12. Case IV. Laminagraphic section through the anterior portion of the lung shows marked vascular distortion about the lesion.

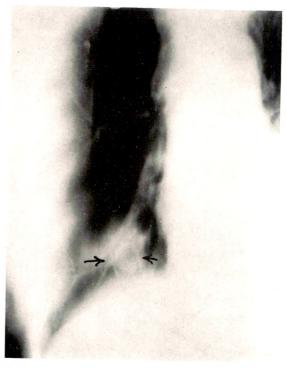


Fig. 14. Case v. Laminagraphic section shows multiple vascular shadows in relation to the lesion. The lateral arrow indicates a vessel curving around the lesion. The medial arrow indicates a "taut" vessel.

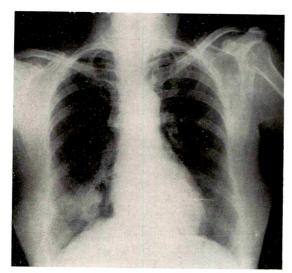


Fig. 13. Case v. A large lobulated dense shadow is seen in the right lower lung on the conventional roentgenogram.

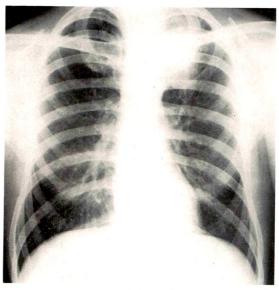


Fig. 15. Case vi. A poorly demarcated density is seen in the left upper lobe on the conventional roentgenogram.



Fig. 16. Case vi. Laminagraphic section shows a vessel curving smoothly about the lateral border of the lesion (arrow).

entire 10 cm. specimen of the left upper lobe was occupied by a tumor mass (squamous cell carcinoma of the lung).

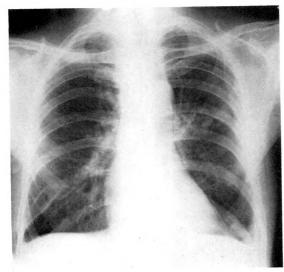


Fig. 17. Case VII. A poorly defined density is seen lateral to the left hilus on the conventional roent-genogram.



Fig. 18. Case vii. Laminagraphic section shows the density with a lucency within it.

Case VII. C.H., a 48 year old patient, had a mass in the neck for a period of 6 weeks and involuntary movements of the arm and leg for 2 days. He developed fever, weakness and tiredness 6 weeks prior to admission.

A conventional chest roentgenogram (Fig. 17) on February 15, 1959 demonstrated a faint infiltrate lateral to the left hilus. A laminagram at 6 cm. (Fig. 18) showed a mass containing a lucent area; and a laminagram at 11 cm. (Fig. 19) showed taut elongated vessels.

Scalene lymph node biopsy revealed secondary carcinoma.

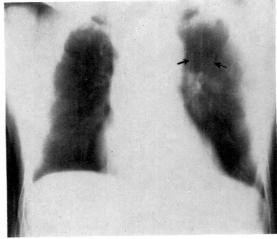


Fig. 19. Case vii. Laminagraphic section 5 cm. anterior to Figure 18 shows 3 "taut" elongated vessels passing vertically into the upper lobe (arrows).

despite considerable delay in resection of a cancer which was small when it appeared 6 months after a negative roentgenogram.

The pertinent data for the 12 cases reported in this paper are summarized in Table I in order of increasing mean diameter of the cancers when first recognized. Age of the men at the time of roentgenologic recognition (a point designated by the symbol X) ranged from 51 to 82 years. Tissue type was squamous cell in 5 instances, undifferentiated in 3, adenocarcinoma in 2 and mixed squamous and adenocarcinoma in 2. Cancer was first recognized roentgenographically from 6 months to 9 years and 2 months after the men had entered the Project. The chest roentgenogram which immediately antedated the X film was taken at an interval which ranged from 5 to 7 months.

The size of the cancer at the time of first recognition varied from 1.0 to 8.2 cm. in mean diameter; half were less than 2.0 cm. Doubling time could be estimated in 8 of the 12 cases from growth curves such as those shown in Figure 3—in 4 by virtue of measurements which could be made retrospectively on roentgenograms prior to the X film and in 4 through measurements made on subsequent studies. Doubling times ranged from 2.0 to 10.0 months, half of them falling between 2.0 and 4.0 months.

By actual retrospective measurement or extrapolation from growth rate curves (see below), the mean diameter of the cancers on the X-I film in 8 cases varied from 0.7 to 2.8 cm. These figures (column 10 in Table I), in general, paralleled the rank order of the mean diameter at X (column 8). The lesions which exceeded 1.0 cm. at X-I were either hazy and ill-defined (3 cases) or obscured by bony structures (rib and clavicle in I case).

It should be emphasized that the X film was the roentgenogram on which the cancer was first recognized and read as such during the prospective execution of the research work. Eight of the 12 X-1 films had been read initially by 2 physicians reading independently; cancer was not suspected by

either reader. Further, all X-I films have been read by panel review. In only I instance (E.B.R.) did a majority of the panel members recognize the cancer in the X-I film in which the lesion measuring 1.45 cm. in diameter was partially obscured by a rib and clavicle.

Only 4 of the 12 men had resections. Surgery was not done in 8 for the following reasons: One (N.M.) had metastases recognized clinically before his primary tumor was detected; 3 refused study; 2 were explored and found to be inoperable; in 2 cases surgery was contraindicated by other extensive pulmonary disease (bullous emphysema in I case and silicosis in the other). In the 4 cases that were resected, surgery was performed within $1\frac{1}{2}$ months in 2 men, delayed for 3 months in 1 man while he was studied for tuberculosis, and delayed for 32 months in the fourth because surgery was thought at first to be contraindicated by advanced age and poor general condition.

This low resection rate may be due in part to the nature of the Philadelphia Pulmonary Neoplasm Research Project. Early, pressure to accept study alienated a number of men. Since the major objective of this Project was a study of the natural history of lung cancer, recommendations are made but undue pressure is not exerted on the men to accept advice even when a suspicious lesion develops roentgenologically.

Six men had forms of therapy other than resection. Two of the 8 unresected cases received radiotherapy; 3, both irradiation and chemotherapy; and I resected case received adjunctive chemotherapy.

Survival from the X film (column 13 in Table 1) ranged from 1 to 50 months and correlated with the diameter of the cancer on the X film. The survival period from the X film is plotted against initial tumor size in Figure 4 for each of the 12 cases. No initial mean diameter was smaller than 1.0 cm. when the cancer was first recognized, suggesting that 1.0 cm. is the minimal detectable size of a pulmonary nodule. This has been indicated on the graph by the interrupted horizontal line. The plotted

DATA FOR 12 MEN WITH MEASURABLE LUNG CANCER 5 TO 7 MONTHS AFTER A ROENTGENOGRAM READ NEGATIVE TABLE I

,,,,	William Weiss, Radianne R. Bodeot and David II. Cooper												
(14)	Remarks	Metastases 1-27-64 to supracla- vicular lymph nodes	Resoction thought to be curative; sutopsy (thous only) showed re- currence and metastasis	Autopay: widespread metastases	6×6 cm. mass in chest wall 2-22-61; a unicellular metastasis would have occurred 18.5 years previously	Pleural extension at thoracotomy	Metastases found Sept., 1958; autopay: carcinomatoris	Autopay: metastares	Metastases found 8-3-58	Resection thought to be curative; no autopsy.	Metastases noted in 14X17 film of 11-28-61 (X minus 6 months); mass in chest wall 5X6 cm. on 1-1-62	Autopsy: metastases and numerous amail pulmonary emboli	Autopsy: no metastases (brain not examined)—death attributed to silicosis and carchoms of the lung
(£13)	E EME	27	S	g	40	8	12	ង	31	'n	4	23	н
(13)	Date Of Death	7-20-64	1-24-65	12-14-58	5-27-61	3-17-63	11-18-58	8-20-56	11-24-58	12-11-55	69-1-6	6-3-63	12-18-56
	Chemo- therapy (NHz)	+				+	+	+					
(11) Therapy	Irradi-				+	+	+	+				+	
F	Resection	Lobectomy 6-13-62	Segmental 7-29-63	ı	-	1	1	1	Pneumo- nectomy 7-31-56	Lobectomy 8-15-55	1	1	1
(ro) Mean	Measured or Extrapolated at X - 1 (cm.)	0.70	88.0	0.05	0.84	r. 60 (faint lesion)	r.rs (faint legion)	1	(behind rib and clavicle)	1	1	2.80 (hany)	
3,	Ting Fig.	4.0	%.o	6.25	4.5	10.0	2.75	ı	2.0	1	ı	3 .0	1
<u></u>	Mean	1.0	1.0	1.2	I.2	1.8	1.9	2. I	2.8	4.4	5.0	5.0	8.3
Size at X (cm.)	Diam- eters	0.9XI.I	0.0XI.2	1.2XI.2	1.1X1.3	1.4X2.1	1.9X1.9	1.2X3.0	2.4×3.5	4.1×4.7	4.7×5.3	4.7×5.3	7.4×8.9
(4)	Type of Film at X	70 mm.	70 mm.	70 mm.	14×17 in.	70 mm.	70 mm.	70 mm.	70 mm.	70 mm.	70 mm.	70 mm.	70 mm.
ල ු	X X X	7	9	9		9	9	4	9	9	9	ъ	9
	×	4-38-63	11-23-60	3-21-57	1-20-58	11-22-60	11-26-57	p-90-54	4-23-56	7-26-55	5-14-62	4-16-62	11-26-56
(s) Dates	X-1 [®]	19-4-01	5-24-60	9-20-56	6-13-57	5-16-60	5-28-57	2-10-54	10-24-55	1-18-55	11-9-11	19-9-11	6-4-56
'	Entry Into Project	1-21-55	10-25-54	5-7-53	4-6-54	11-23-54	10-27-53	6-11-53	3-27-54	1-18-55	6-29-55	2-36-53	6-7-55
3	Cell Type	Undiffer- entiated	Adeno- carcinoma	Mixed	Squamous	Adeno- carcinoma	Squamons	Undiffer- entisted	Mixed	Squamous	Undiffer- entiated	Squamous	Squamous
3	ž=X	52	2	đ	88	53	31	39	57	99	83	59	51
3	No.	4999	4639	2304	3712	4737	2914	2484	3667	4080	5768	8201	3661
Ξ	Case	D.A.M.	J.F.S.	J.G.M.	a a	S.B.M.	H.S.S.	F.Y.	E.B.R.	M.R.	N.M.	W.I.	J.H.

points describe a crescent-shaped area, the concave border of which may be called a lethal boundary20 because it defines the maximal possible duration of life for cancers with various growth rates as indicated by size 6 months after a negative roentgenogram. The 4 men with cancers larger than 4 cm. survived only I to 13 months while the 8 men with smaller cancers survived from 12 to 50 months. Thus, there is an inverse relationship between length of survival and initial tumor size 6 months after a roentgenogram read as negative. Resection did not seem to alter this relationship although our series is too small to justify definite conclusions in this regard. The man who lived the longest (J.F.S.) had one of the smallest tumors at the time of detection. He survived 50 months despite a 32 month delay in resection.

In Table II survival is related to initial tumor size according to tissue type. The inverse relationship between survival and initial tumor size held for each histologic category except for the 2 cases of mixed squamous and adenocarcinoma. Resection may have accounted for the longer survival of the man with the larger tumor. Because



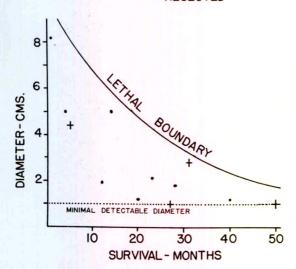


Fig. 4. Survival of 12 men with lung cancer according to the initial size of the tumor 5-7 months after a roentgenogram read as negative.

TABLE II

SURVIVAL OF MEASURABLE LUNG CANCERS BY TISSUE
TYPE IN ORDER OF INCREASING DIAMETER
5-7 MONTHS AFTER A ROENTGENOGRAM
READ AS NEGATIVE

Cell Type	Diameter (cm.)	Re- sected	Survival after first roent- genogram read as cancer (mo.)
Squamous			
F.E.	I.2		40
H.S.S.	1.9		12
M.R.	4.4	+	5
W.I.	5.0		13
J.H.	8.2		I
Und ifferentiated			
D.A.M.	1.0	+	27
F.Y.	2.1		23
N.M.	5.0		4
Adenocarcinoma			
J.F.S.	1.0	+*	50
S.B.M.	1.8		28
Mixed			
J.G.M.	1.2		20
E.B.R.	2.8	+†	31

* 33 months after first roentgenogram read as showing cancer. † 3½ months after first roentgenogram read as showing cancer.

of the small number of cases in each histologic group, no comparisons could be made.

We have made the assumption that the size of the cancer roentgenographically 6 months after a roentgenogram read as negative reflects the rate of growth. This assumption is supported by actual measurements of growth rate in the 8 cases for whom appropriate data are available. First, it can be shown that growth rates are reasonably constant. Figure 3 is based on 4 cases which had 3 or more roentgenograms on which tumor diameters could be measured. Second, in the 8 cases for which growth rates were estimated by calculating doubling times, there is a rough inverse relationship between growth rate and duration of survival (Fig. 5) just as there was between initial size and survival (Fig. 4). Figure 6 shows a direct relationship be-

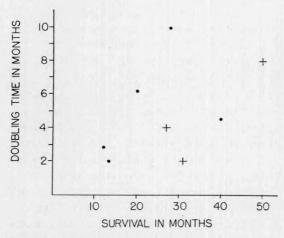


Fig. 5. Survival of 8 men with lung cancer according to the doubling time of the tumor.

tween initial size and growth rate although with semiannual roentgenograms shows up only for those cases having the more rapid growth rates.

DISCUSSION A. METHOD

Certain difficulties are inherent in the method used in this study. First, the findings are derived from data on lung cancers located peripherally which grew in a spherical form and had reasonably sharp borders. In our experience, this is characteristic only of one-third of bronchogenic carcinomas so inferences drawn from such data may not

apply to all lung cancers.

Second, the accuracy of measurements of diameters varies. The margin of error is large with small lesions because the borders seem less sharp under magnification. This error decreases as size increases. However, with growth, the shadow of the tumor may not enlarge equally in all directions so that mean diameter must be determined and may not reflect the true growth rate. It might be postulated that maximal diameter would be more accurate. However, this did not prove to be so in this small series.

Finally, recognition of the earliest roentgenographic shadow of the cancer suffers from considerable inaccuracy. Greening and Pendergrass¹¹ pointed out in 1954 that even large cancers (2-5 cm. in diameter)

may occasionally be missed on chest roentgenograms if they are located in "blind" areas, e.g., along the parietal pleura, close to ribs, or in the midline. The lower limit of resolution on chest roentgenograms in the course of routine study is probably 1.0 cm. Spratt et al.18 found that radiologists were able to locate the shadows of lucite balls regularly only if they measured 1.0 to 1.2 cm. in diameter. They could recognize the lucite balls of 0.6 cm. in diameter only when located in intercostal spaces in contrast to aerated lung. Balls as small as 0.3 cm. could be identified only in retrospect.

Goldmeier¹⁰ stated that a cancer less than 1.0 cm. in diameter cannot be diagnosed roentgenologically with standard methods. Our experience confirms this. Goldmeier considered three factors to explain this phenomenon: (1) rapid growth if a tumor grows very rapidly then serial roentgenograms must be taken at short intervals to provide sufficient opportunity to reveal the lesion when it first reaches visible size; (2) signal-to-noise ratio—a lesion must achieve a size and density which will permit its shadow to be distinguishable from background shadows of normal structures; and (3) density—the periphery of a tumor is not as dense as its

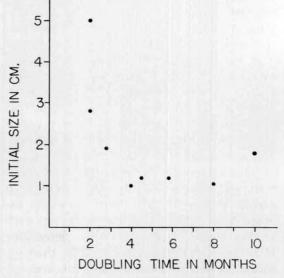


Fig. 6. Initial size of tumor according to doubling time in 8 men with lung cancer.

central portion; since the periphery is relatively large in small spherical lesions, smaller tumors are more difficult to visualize than are larger tumors. The apparent density of a lesion depends on the quality of the roentgenogram: overpenetration may "burn out" a faint tumor shadow while underpenetration may reduce the signal-to-noise ratio.

It is common knowledge that a small faint nodule may be visible in retrospect when it was not discernible prospectively. Since retrospection introduces bias which varies in degree from one observer to another, prospective recognition of the neoplasm has been used in our study to determine the first roentgenogram on which the tumor became visible. This approach has the additional virtue of being realistic in that it is based on the recognition of cancer under actual field conditions in contrast to the retrospective approach of Rigler¹⁶ and Emerson *et al.*⁸

B. SURVIVAL OF PATIENTS WITH BRONCHOGENIC CARCINOMA ORIGINATING AS SOLITARY NODULES

Survival for patients with malignant solitary nodules appears to depend primarily on resection. Series limited to resected cases have fairly good survival rates. For example, 46 per cent of 280 resected cases reported by Steele²² survived 30 months. All of Steele's cases were derived from hospitalized veterans. In contrast, in a series such as that reported by McClure et al.14 which was derived from a fast-tempo community survey, only 6 of 13 cases were resected; 4 (31 per cent) survived 30 months and 2 (15 per cent) lived 5 years. Are these differences in survival actually due to resection or is case selection an important factor; i.e., is the better survival of resected patients due, to some extent, to a higher proportion of individuals predisposed to survive by some other factors such as slower growth rates or earlier detection? If earlier detection is important, then we would expect a good inverse relation between size of cancer at discovery and survival.

C. SURVIVAL OF LUNG CANCER PATIENTS WITH
SOLITARY NODULES IN RELATION TO SIZE OF
CANCER AT DISCOVERY

The information in the literature on the relationship between survival and cancer size at time of detection is conflicting. Guiss and others 12,23,25 were unable to find a significant correlation in almost 200 resected cases. Bateson¹ reported 3 year survival as 54 per cent for 47 cases with cancers of less than 5 cm. diameter and 20 per cent for 17 cases with cancers 7 cm. or larger. Steele²² found that the 30 month survival rate was 52 per cent for 177 cases with cancers of less than 3.0 cm. diameter and 38 per cent for 114 cases with cancers 3.5-6.0 cm. diameter. The differences reported by the last two investigators are statistically significant (P < 0.05) though relatively small. The lack of consistency in the literature suggests that the size of cancer at any particular time alone, as distinguished from change in size per unit time, is not closely related to survival.

D. SURVIVAL IN RELATION TO GROWTH RATE

In 1935 Mottram¹⁵ reported that both benign and malignant warts produced by the application of tar to the skin of mice have very constant growth rates from the time they become of macroscopic size. When size is plotted logarithmically against time, the curve is a straight line. The fact that the length of the invisible growth phase is related to the rate of growth measured in the visible phase and is longer with slower growth rates suggests that invisible growth is also constant. Brues et al. 6 showed that in mice almost all the latent period between initial application of carcinogens and the time when a tumor was first palpated could be accounted for by assuming that neoplasia begins with a relatively small number of malignant cells and has a constant growth rate. The latent period varied inversely with the rate of growth measured during the macroscopic growth phase; the growth rate varied directly with the mitosis count. More recently, Bertalanffy and Lau² presented experimental

evidence that there is a constant increase in the number of malignant cells each day during the period of active growth of transplantable neoplasms until the onset of necrosis.

The doubling time hypothesis makes the following assumptions: the origin of a cancer is unicellular, or nearly so; the growth rate is geometric and constant. If we accept these assumptions, then the rate of growth can be described as the time required for the volume of a given neoplasm to double. When a tumor doubles its diameter, its volume increases by a factor of 8 since 3 doublings of the volume occur (1–2, 2–4, 4–8). As diameter increases, volume is cubed. The number of cells is approximated by volume rather than by diameter.

A single malignant cell of 10 µ diameter will produce a nodule I mm. in diameter in 20 doublings and 1 cm. in diameter in 30 doublings. Ten more doublings create a mass of approximately 1 kg. and only a few more doublings would produce an unsupportable amount of tumor tissue so death must supervene soon after 40 doublings.7 If this hypothesis is valid, then, knowing the doubling time, (1) the time of the cancer's onset from the initial malignant cell can be extrapolated, (2) the time of the host's death can be predicted if the disease is not eliminated, (3) deviation of the observed course from the predicted curve may be used as a measure of the efficacy of nonsurgical therapy, (4) the maximum period for risk of recurrence or appearance of metastases can be computed following an attempt at curative therapy (if I cell remains, knowing the doubling time, one can calculate the period that will elapse till the time the cell produces a nodule I cm. in diameter), and (5) if metastases are already present, the time of their implantation can be estimated.

Since most cancers are not detected until they have grown to a diameter of I cm., two-thirds to three-fourths of their lifetime has been invisible or preclinical so metastases may well occur before the tumor reaches clinically recognizable size. This does not alter the correlation between growth rate and survival because there is experimental evidence that metastatic potential varies directly with the rate of growth. The implications for the concept of "early" detection are obvious.

Some evidence has been accumulated to support the applicability of the doubling time hypothesis in its broad outlines to the course of human cancers.^{7,9,17–21} If established firmly, this explains certain observations on the course of neoplasia outlined in part by Collins *et al.*:⁷

(1) The occasional inadequacy of the arbitrary 5 year cure period in common use. Slowly growing neoplasms may require many years to reach a discernible size.

- (2) The long duration of invisible growth (often years) explains the failure of early roentgenologic detection to influence survival in many reported series since diagnosis is not early in the light of the many doublings which have occurred by the time the tumors are visible.
- (3) Currently, therapy is offered only during the final third or quarter of the cancer's course. Many therapeutic failures are due to metastases already present when therapy is instituted. The late appearance of metastases, even after years of survival without evidence of persistent disease at the treated primary site, does not require the concept of dormant cancer cells. A doubling time of 100 days, a common occurrence, would mean that a 1 cell metastasis would require 8 years to grow to a 1 cm. nodule, assuming a constant growth rate.
- (4) The impression of sudden rapid increase in cancer size is an illusion. When volume increase is plotted arithmetically, there seems to be an increasing rapidity of growth. The fact is that the rate of change is constant; when volume increase is plotted logarithmically, the curve is a straight line.

Incidents such as hemorrhage, therapy, the outstripping of nutritive supply with resultant necrosis, and metabolic or hormonal alterations may change the constancy at which a particular cancer grows. Furthermore, the non-neoplastic portions (stroma and vessels) of a tumor may be significant in relation to growth rate and may not have the same growth pattern as the malignant portion. It must be recognized that our data and those of other investigators^{7,9,17–21} are only approximations.

When we plotted survival by initial size for the 12 cases reported in this paper (Fig. 4), the points fell into a crescent-shaped area such that men with large tumors survived a short period but the men with small tumors survived for longer but variable periods. This phenomenon is readily explained by the doubling time hypothesis. In Figure 7 the hypothetical diameters of 3 lung cancers have been plotted against time between a negative roentgenogram and an abnormal one 6 months later according to growth rate and the time the cancer reaches detectable size (set at I cm.). Curve A describes the increase in diameter for a rapidly growing tumor with a volumetric doubling time of I month if it first becomes detectable I week after the negative roentgenogram—the diameter on the next roentgenogram will be approximately 4 cm. Curve B describes the increase in diameter of a slowly growing tumor with a doubling time of 3 months if it also first becomes detectable I week after a negative roentgenogram-its diameter on the next roentgenogram will be only 1.6 cm. If a rapidly growing tumor with a doubling time of I month first becomes detectable 4 months after a negative roentgenogram, then Curve C results and this tumor will also have a diameter of only 1.6 cm. on the roentgenogram 6 months later. Thus, a tumor which is large when first seen in semiannual chest roentgenograms must be growing rapidly, but a tumor which is small may be growing rapidly or slowly.

E. RESECTION IN PERSPECTIVE

Extirpation is the only therapy accepted as significantly effective for lung cancer. However, resection is limited to a minority

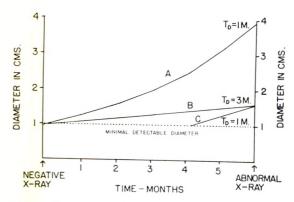


Fig. 7. Hypothetical growth curves, plotted on an arithmetic scale, according to growth rate and time of detection in relation to chest roentgenograms taken at a 6-month interval. Curves A and C illustrate a rapidly growing cancer while Curve B illustrates a cancer with a moderate rate of growth. T_D is doubling time and M. is month(s).

of the total number of cases. Some patients defer or refuse operation. Others have cancers too far advanced to permit surgical management and still others suffer from nonmalignant conditions (e.g., old age, poor pulmonary reserve or cardiac insufficiency) that contraindicate resection. Enthusiasts have argued that surgical therapy must be applied "early" and have criticized the months of delay which sometimes occur, whether the delay is due to the patient or to the physician. This attitude of urgency is contradicted by the occasional patient who survives 5 years or more without resection.

There are cogent reasons in the present state of our knowledge to question the urgency for resection in bronchogenic carcinoma. For example, Tala and Virkkula²³ studied the interval from diagnosis or onset of symptoms to resection in 97 cases and found no notable differences in survival rates in relation to length of delay. In our own analysis of over 1,500 cases of proved bronchogenic carcinoma in the Philadelphia County Medical Society study²⁴ and in cancers found by official Philadelphia surveys,³ survival has been poorer for patients with little or no delay than for patients with greater delay.

The data presented in this report suggest that survival may be largely predetermined

by the biologic characteristics of each carcinoma, e.g., rate of growth, and even if all other conditions are favorable for resection, such therapy may be effective only in patients whose tumors are growing so slowly that there is opportunity to find them by serial chest roentgenograms while they are still small and have not metastasized.

SUMMARY

Seventy-six proved cases of bronchogenic carcinoma developed during an 8-10 year follow-up period among 6,137 older men in the Philadelphia Pulmonary Neoplasm Research Project. Twelve of these men had measurable peripheral tumors, chest roentgenograms read as negative 5 to 7 months before the first roentgenograms on which cancer was recognized, and survival was apparently determined only by the malignant disease. Four cases were resected. The initial size of the cancer ranged from 1.0 to 8.2 cm. in mean diameter; there was an inverse correlation between initial size and survival, whether the tumor was resected or not.

The initial size of a cancer 6 months after a chest roentgenogram read as negative reflects the rate of growth. This was confirmed in 8 cases by an inverse correlation between initial size and doubling time.

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LUNG SCANS WITH I¹³¹ LABELLED MACROAGGRE-GATED HUMAN SERUM ALBUMIN (MAA)*

By JEROME D. SUTHERLAND, M.D., GERALD L. DENARDO, M.D.,† and DONALD W. BROWN, M.D. DENVER, COLORADO

AGGREGATION of radioactive human serum albumin was first used in studies of phagocytosis,1 but recently has achieved wider usage in radioisotope lung scanning. When albumin is heated in an alkaline solution, a colloidal suspension of particles less than I micron in diameter is formed. Injected intravenously, these particles are rapidly engulfed by the reticuloendothelial system, principally within the liver. If, instead, aggregation is carried out at a pH of 5.5, particles 10 to 50 microns in diameter are formed. These so-called macroaggregated human serum albumin (MAA) particles exceed the 7 micron diameter of the average pulmonary capillary, and are filtered out of the blood and trapped within the lung following intravenous administration. If the MAA is labelled with a radioisotope, scanning of the chest will provide a picture of the peripheral pulmonary artery distribution.

In recent months encouraging reports have appeared in the literature describing the use of lung scanning in cases of pulmonary emboli, 4-8.10 bronchogenic carcinoma, and subphrenic abscess. Abnormal lung scans have also been reported in patients with pulmonary abscess, emphysema, blebs, pneumonia, atelectasis and sequestration. 4

The following is a report of the findings in 153 consecutive lung scans performed on 135 patients at the University of Colorado Medical Center and Fitzsimons General Hospital in Denver between January 7, 1963 and May 1, 1965.

METHODS

Patients were given 5-20 drops of saturated solution of potassium iodide orally to block the thyroid. The MAA was stored at 5° C. to prevent breakdown in particle size. Three-hundred microcuries of I131 tagged MAA were injected intravenously and scanning begun immediately. Commercially available scanners equipped with 3 inch sodium iodide, thallium-activated crystals and 19 hole collimators were used. Scanning speeds varied from 30-50 cm. per minute and line spacing was 0.4 cm. Scanning was performed with the patient in the prone position when his condition permitted. Many patients, however, were too ill or uncomfortable to tolerate this position for the approximately 45 minutes necessary to complete a lung scan and in those the supine position was used. The prone position facilitates evaluation of the retrocardiac portion of the left lower lobe. Quinn4 has suggested scanning cephalad from the lower lung margin to avoid the confusion caused by increasing activity in the liver and spleen. This has not been a problem for us, but, in view of the higher incidence of emboli in the lower lungs, we generally scan in this manner. For comparison purposes, a 72 inch supine chest roentgenogram was taken during regular breathing.

RESULTS

ACUTE PULMONARY EMBOLISM

Of the 153 scans, 71 were requested for evaluation of possible acute pulmonary embolism. One was technically unsatisfac-

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tory and is not considered further. Results of the lung scans were correlated with the clinical diagnosis and chest roentgenogram. The report in the patient's clinical record at the time of each examination was used to evaluate the scans and chest roentgenograms. The clinical diagnosis was based on the final impression in the clinical chart, electrocardiographic findings, whether or not anticoagulants were used, LDH values and the clinical course. In addition, 4 patients had pulmonary arteriograms and autopsies were performed on 4 patients.

Thirty-nine scans were interpreted as consistent with pulmonary embolism. Of these, 17 were in agreement with the chest roentgenogram and clinical course. Thirty-one scans were interpreted as negative for pulmonary embolism and in 13 of these, the roentgenogram and clinical course were also not consistent with embolism. These figures show that the scan, roentgenogram and clinical diagnosis agreed in 30 cases (43 per cent).

Of more interest are the 40 instances (57 per cent) in which the scan interpretation conflicted with the roentgenographic interpretation or clinical course or both (Table

1). In 22 of these patients (31 per cent), the scan was probably correct while the roent-genogram was in error. In 10 (14 per cent) of the 22 cases the scan and clinical course were both strongly suggestive of pulmonary embolism while this diagnosis was not recorded in the corresponding roentgen interpretation. Two of these patients were proven to have pulmonary embolism at autopsy, performed 6 and 7 days, respectively, after the scan (Fig. 1, A and B) and 1 had a pulmonary arteriogram suggestive of embolism.

In each of the remaining 8 cases, the scan and clinical course were against pulmonary embolism while the roentgenogram was interpreted as showing evidence of pulmonary embolism or infarction. Seven of these cases were found to have bronchopneumonia and I had pulmonary edema. It has been previously recognized that bronchopneumonia without consolidation produces no defect in the lung scan.⁴

In 18 patients (25.5 per cent), the scan appeared superficially to be in error—8 false positives and 10 false negatives. Evaluation of these cases individually, however, reveals that most of these mis-

Table I

SUMMARY OF 70 LUNG SCANS REQUESTED FOR EVALUATION OF ACUTE PULMONARY EMBOLISM

Clinical	Scan	Roentgenogram	No. of Cases	Total	Per Cent	Scan Results	
+	+	+	17				
			13	30	43	Correct and in agreemen	
+	+		14			C	
- 1		+	8	22	32	Correct	
+	-	-	8				
+		+	2	10	15	False negative*	
	+	+	7	0	10	False positive*	
4-14	+	_	I	8			

^{*} Although the final clinical diagnosis is assumed to be correct, it is probable that in several of these patients, the scan was correct while the clinical diagnosis was in error.

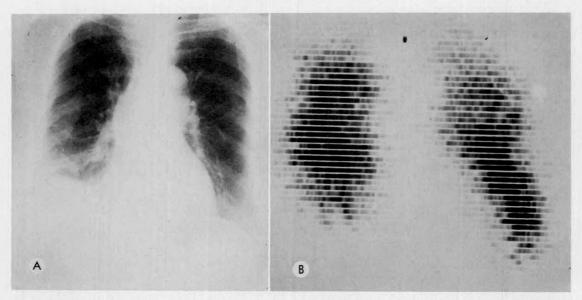


Fig. 1. (A and B) Pulmonary emboli. Decrease in scan activity in the right lower lung and on the left lateral lung margin in the form of a crescent. Proven to have bilateral pulmonary emboli at autopsy 7 days later.

leading results can be explained by unusual clinical situations or by the fact that scanning was performed before or sometime after the probable occurrence of the acute embolization.

In 8 of the 10 patients classed as false negatives, roentgenographic interpretations were negative for embolus while the clinical impression was positive. Five of these patients were anticoagulated for thrombophlebitis and were diagnosed as possible pulmonary emboli but did not fulfill many of the criteria for this diagnosis. Another had a good clinical picture of pulmonary embolus post partum and I was proven to have multiple pulmonary emboli at autopsy. The latter's scan was difficult to interpret because of a right pneumonectomy and hyperexpansion of the left lung. The 8th patient had diffuse pulmonary emphysema which resulted in a scan that was difficult to evaluate for decreased activity due to embolism. In the other 2 cases showing false negative results, the roentgenogram and clinical impression were positive while the scan was negative. In one of these the roentgenogram showed only minimal pleural effusion. In the other, the patient had a clinical acute embolus 12 days prior to the scan. The thrombus may have recanalized by the time the scan was performed as has been shown by Wagner *et al.*¹⁰ to occur in dogs.

In 7 of the 8 scans classed as false positives, both the roentgenogram and scan interpretations were positive while clinically the patient did not have an embolus. Five of these had pneumonia, I had bullae and pneumonia and I had bullous emphysema. In the other false positive case, the clinical and roentgenographic evaluations were negative for embolism while the scan was interpreted as being compatible with embolism. This patient had diffuse emphysema.

It is worth noting that in several patients with pulmonary emboli, the scan revealed a lack of pulmonary artery circulation in areas in addition to those showing increased densities on the roentgenogram, thus demonstrating undetected multiplicity of embolization.

OLD PULMONARY EMBOLISM

Eleven scans were performed on patients who had well documented pulmonary emboli sometime prior to the current examination. Results in these patients were vari-

able. One scan showed considerable return of perfusion to the area of embolism in $2\frac{1}{2}$ months (Fig. 2, A and B). Another, 2 years after clinical infarction, showed a marked decrease in activity in the left lower chest. This patient, however, had accompanying pulmonary hypertension. Another case was negative I year after clinical infarction and 2 others 5 years after clinical infarction.

COMBINED LUNG-LIVER STUDIES

Brown² has combined lung and liver scans in order to demonstrate the right subphrenic space. Twenty-eight patients in the present series were given 1.7 μ c per kilogram of Au¹⁹⁸ colloid intravenously in addition to 300 μ c of I¹³¹ labelled MAA. Scans were made to include both the lungs and liver. Four patients were subsequently proved to have subphrenic abscesses. Another patient had 450 cc. of sterile fluid in the subdiaphragmatic space, which represented a chronic hepatic subcapsular hematoma secondary to trauma 5 months previously (Fig. 3, A, B and C). All of these cases were quite apparent on the combined

lung-liver scan. There were no false negative studies in this group and no false positive studies in the 23 patients who did not have disease in the subdiaphragmatic space. In I case, colon interposition between the liver and diaphragm was present. This finding, readily apparent on the roentgenogram, was taken into account in the negative scan interpretation.

PULMONARY NEOPLASMS

Wagner and associates9 described a disproportionate decrease in activity in lung scans of patients with broncho-occlusive carcinoma. In our 7 patients with primary bronchogenic carcinoma, Wagner's impressions were confirmed. Three patients showed complete lack of activity in the hemithorax containing the bronchial lesion (Fig. 4, A and B). The other cases showed decreased or absent activity in the lobar distribution of the occluded bronchus. In scans of 2 cases with metastatic carcinoma, one showed defects corresponding to the roentgenogram and the other was normal. This was expected since the metastatic lesions were less than 2 cm. in diameter.

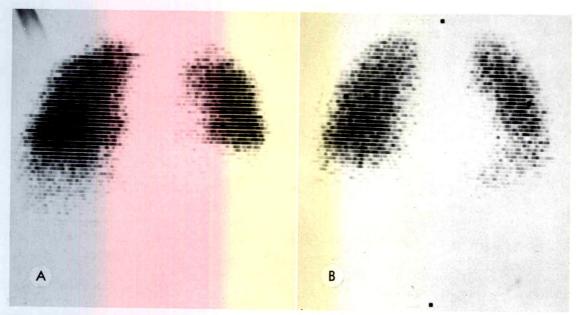
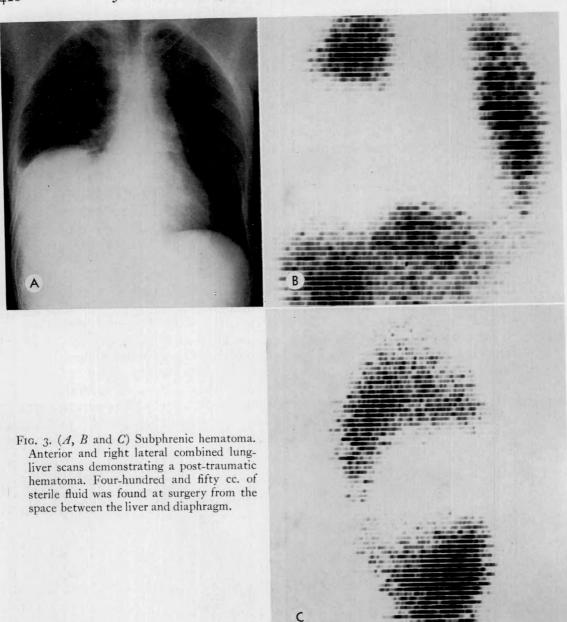


Fig. 2. (A and B) Follow-up of pulmonary embolism (posterior scans). (A) Scan shows decreased activity in the left lower lung 2 days after acute pulmonary embolism. (B) Scan made $2\frac{1}{2}$ months later demonstrates partial revascularization.



PULMONARY EMPHYSEMA AND BULLAE

Sixteen studies were performed on patients with generalized or bullous emphysema. Five of these patients were known to have pulmonary hypertension including I who had an atrial septal defect. Bullae were apparent as areas of decreased activity in the lung scans (Fig. 5, A and B). Diffuse emphysema caused an

irregular decrease in lung activity and increased uptake in the liver (Fig. 6, A and B). However, one cannot rely on the latter finding since the liver uptake depends greatly on the number of small particles in the particular batch of MAA. Pulmonary atrioventricular shunting has been thought to occur in diffuse pulmonary emphysema and has recently been con-

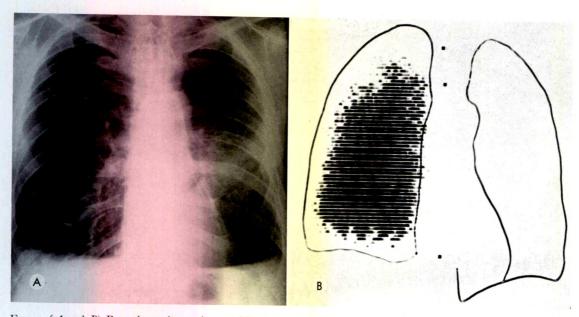


Fig. 4. (A and B) Bronchogenic carcinoma. The lung scan shows absence of activity on the left. A left hilar mass is present which on arteriography occluded the left main pulmonary artery.

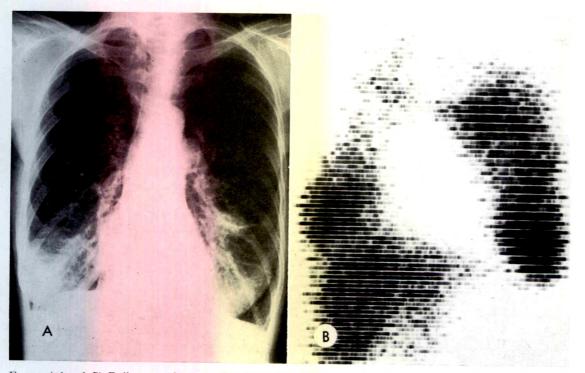


Fig. 5. (A and B) Bullous emphysema. Combined lung-liver scan showing decreased activity in the upper lungs due to large bullae.

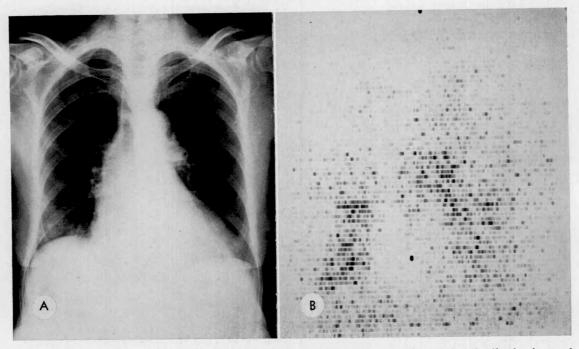


Fig. 6. (A and B) Diffuse emphysema. A marked decrease in lung activity with irregular distribution is noted on the scan. There is more activity in the region of the liver than is usually seen.

clusively demonstrated by pulmonary wedge arteriography.³ Distortion of pulmonary vascularity by hyperexpansion with resulting irregularly decreased concentration of MAA produces the abnormal scan.

MISCELLANEOUS CHEST DISEASES

Active infiltrative tuberculosis caused defects in the scan as did chronic changes including cavities, significant calcification, and fibrosis. A case of Goodpasture's syndrome showed a slight decrease in density not unlike that seen in pulmonary edema. A case of mild pulmonary edema showed no scan abnormality. A case of mitral stenosis showed a relative decrease in blood flow to the lower lung zones (Fig. 7). In a

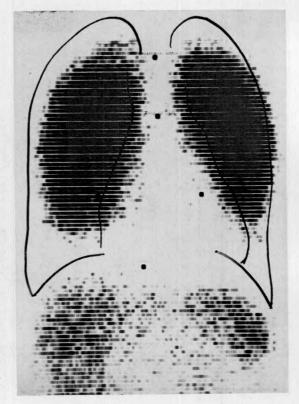


Fig. 7. Mitral stenosis. Lung scan demonstrating decreased vascular perfusion in the lower lung zones and arteriovenous shunting resulting in increased liver and spleen activity.

A REACTION FOLLOWING ADMINISTRATION OF MACROAGGREGATED ALBUMIN (MAA) FOR A LUNG SCAN*

By HOWARD J. DWORKIN, M.D.,† JOSEF R. SMITH, M.D.,‡ and FRANCES E. BULL, M.D.§ ANN ARBOR, MICHIGAN

THE radionuclide perfusion lung scan has been studied in various animals and has been shown to be a suitable indicator of relative pulmonary blood flow.2,11,14 In patients with various forms of pulmonary vascular occlusive disease, the lung scan has vielded useful information and has been shown to correlate closely with pulmonary angiography, pulmonary function studies, and postmortem findings.^{3,7,10,14}

The perfusion lung scan is performed by the intravenous injection of macroaggregated albumin (MAA) tagged with I131. The MAA particles employed may range in diameter from about 1 μ to 100 μ with a mean of about 10–30 μ. Their size depends upon the method of preparation. 12,14 The amount of radioactivity given is usually $300 \mu c \text{ of } I^{131}$.

The simplicity, speed, and apparent lack of toxicity have caused rapid acceptance of the lung scan as a clinically satisfactory indicator of relative pulmonary blood flow, particularly as applied to patients with suspected pulmonary emboli.3,14 Although the possibility of adverse reactions has been discussed,3,12,14 none has been reported to our knowledge. The following case is that of a patient who experienced a life-threatening reaction immediately following the intravenous injection of MAA for a lung scan, appeared to recover to her pre-scan status, and died 26 hours later.

REPORT OF A CASE

In May, 1963, W.M., a 36 year old white woman, had a right radical mastectomy, intravenous triethylene thiophosphoramide and prophylatic oophorectomy for adenocarcinoma of the breast metastatic to 1 of 6 axillary lymph nodes, followed by radiation therapy to the right chest, axilla, and supraclavicular fossa. Local recurrence was noted on her chest wall in April, 1964, which was resistant to chemotherapy.

By April, 1965, her chest wall was involved by cancer en cuirasse anteriorly with a fungating mass and the chest reontgenogram demonstrated a small amount of right pleural effusion. Over the course of I week in May, 1965, she became acutely dyspneic on exertion. Roentgen examination revealed complete opacification of the right hemithorax due to pleural effusion containing adenocarcinoma cells. Thoracenteses and intrapleural injections of quinacrine hydrochloride caused apparent cessation of fluid formation. On roentgenographic examination there was opacification of the periphery of the lung, apparently due to pleural thickening and loculated fluid. Pulmonary function tests revealed a reduction of vital capacity (Table 1). Subsequent to this therapy, she had complete relief of exertional dyspnea until early September, 1965, when she again noted mild dyspnea and a feeling of restriction of the right chest. A pulmonary parenchymal nodule at each base now was visible on the chest roentgenogram. The dyspnea was slowly progressive over the next month to the point of 3-flight dyspnea and in late September, she began experiencing acute episodes of hyperventilation accompanied by anxiety and giddiness. Examination at this time revealed the ulcerating, fungating tumefaction of the right anterior chest with nodular tumefaction of the right posterior chest, right supraclavicular fossa, left breast, and lymphedema of the right arm. Respiratory rate at rest was 22 and unlabored. Blood pressure was 120/70,

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T	ABLE I	
PULMONARY	FUNCTION	STUDIES

Predicted Normal	Patient's Values 6-3-65	Patient's Values 10–5–65
2,875 ml.	1,480 ml.	1,360 ml.
	1,045 ml.	855 ml.
	435 ml.	510 ml.
3,815 ml.		2,945 ml.
22.6 ml./min. mm. Hg	g	8.4 ml./min. mm. Hg
	Normal 2,875 ml. 3,815 ml.	Normal 6-3-65 2,875 ml. 1,480 ml. 1,045 ml. 435 ml.

pulse rate 128, weight 111 pounds, and height 62 inches. The left lung was normal to examination, but there was dullness to percussion and bronchial breath sounds on the right. The liver was not palpable. There was neither cyanosis nor clubbing. Laboratory determinations included normal values for the peripheral blood cell counts and differential, urinalysis, blood urea nitrogen, fasting blood sugar, total proteins and A/G ratio, bilirubin, alkaline phosphatase, and calcium. Pulmonary function tests revealed reduction of lung volume and a decrease in diffusing capacity (Table 1). On October 7, she was started on dexamethasone 0.75 mg. t.i.d. in an attempt to palliate what was felt to be symptomatic lymphangitic spread of the carcinoma in the lung. By October 14, she had severe dyspnea on level walking and the dexamethasone was increased to 1.5 mg. t.i.d. By October 17, she was comfortable only at bed rest, with minimal exertion producing dyspnea. A chest roentgenogram at this time (Fig. 1) demonstrated an increase in prominence of the left pulmonary artery shadow and the possibility of recurrent pulmonary embolization as a cause of her dyspnea was reconsidered. She was readmitted at this time and it was necessary to use oxygen by mask intermittently. On October 20, she needed oxygen almost continuously. That morning the lung scan was performed. Within I to 2 minutes after intravenous injection of 300 µc of MAA I131 (11 mg. of albumin, Table II), she complained of faintness and became cyanotic, diaphoretic, agitated, and tachypneic. The initial pulse rate was 80 and rose to 140. The blood pressure was 100/80. There was increased venous pressure as evidenced by engorgement of the neck veins. She responded to oxygen therapy with relief of her profound dyspnea and cyanosis. An electrocardiogram 40 minutes later revealed sinus tachycardia and evidence of incomplete right bundle branch block compatible with acute cor pulmonale though previous tracings were not available for comparison. Blood gas studies were obtained (Table III) and the scan was recorded (Fig. 2). By that afternoon, she was back to her previous state of dyspnea at rest, receiving oxy-

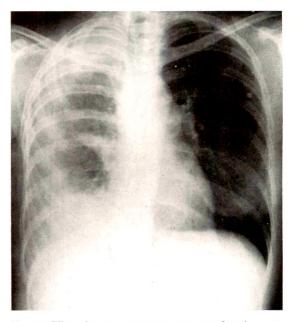


Fig. 1. The chest roentgenogram on October 18, 1965 demonstrates pleural thickening and fluid in the right hemithorax, nodules at right and left bases, a prominent pulmonary outflow tract, and calcified hilar and left upper lobe parenchymal densities.

TABLE II
MAA PROPERTIES

Product -	Mean Per Cent±S.D. in Each Particle Size Range								Approxi- mate	Mean Patient Dose	
	<5**	5-10	10-20	20-30	30-40	40-50	50-70	70-100	>100	Specific Activity $\mu c/mg$.	(range) mg./kg.
*A	47·7 ± 14·5	21.5 ±7.4		6.6 ±4.0		2.6 ±2.3	I.2 ± I.I	I.0 ±2.0	°.3 ±°.5	1,000	0.014 (0.041- 0.003)
*B	17.7 ±14.3	19.3 ±9.4	28.5 ± 12.5		_	-	4.0 ±5.1	I.4 ±2.9	0.2 ±0.8	100	0.09I (0.276– 0.020)
B (Patient W.M.)	4	8	14	12	13	14	20	II	4	100	0.219

^{*} Eleven lots each of Products A and B were examined: 24 lung scans were performed using Product A, and 23 were performed using Product B.

** Particle size (greatest diameter), in microns, was measured visually using a calibrated hemocytometer,

gen by mask, with a temperature of 100.2°F. The dexamethasone was increased to 3 mg. t.i.d. Slowly progressive dyspnea and mild cyanosis were noted during the night. The following morning, her temperature rose to 101°F., she developed pronounced increase in dyspnea, and complained of anterior chest aching. Her blood pressure became unobtainable, her pulse

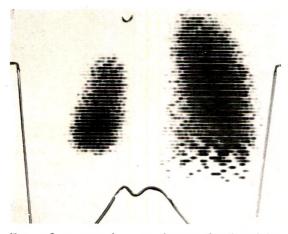


Fig. 2. Lung scan shows an absence of radioactivity in the peripheral portion of the right hemithorax, compatible with loculated pleural effusion. There is relative decrease in activity in the upper half of the visualized portion of the right lung. Note that despite massive generalized tumor embolization, there is a uniform distribution of radioactivity on the left.

slowed, and she expired.

Autopsy. Grossly, there was external tumefaction of the right chest described above. The right lung weighed 280 gm., was firm, contracted, and lacked crepitance. It was covered by thickened visceral pleura, which was densely adherent to parietal pleura anteriorly, inferiorly, and apically. Posterolaterally, there was a 500 cc. unilocular effusion. The left lung weighed 380 gm., and had normal crepitance. The right hilar lymph nodes and adjacent costal cartilages were grossly involved with tumor. Several I cm. pulmonary parenchymal nodules were present in the left base and one 1.5 cm. nodule in the right base. Small metastatic nodules were noted on the parietal pericardium, dome of the liver, pelvic peritoneum, and in 2 dorsal vertebral bodies.

Microscopically, in all sections of both lungs the blood vessels and lymphatics of every size contained clumps and plugs of adenocarcinoma, frequently mixed with small amounts of thrombotic material (Fig. 3, A and B). The large pulmonary arterial branches contained similar clumps. There were focal areas of acute edema and hemorrhage.

Postmortem analysis of the radioactivity concentration was performed by counting samples of lung in a well counter. The right lung samples were found to contain 0.0083 per cent of the administered dose of I¹³¹ per gram of tissue, while the left lung samples were found to

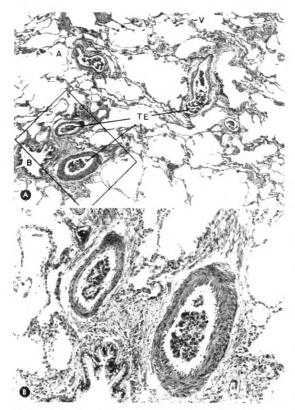


Fig. 3.(A) A representative section of peripheral lung reveals clumps of adenocarcinoma cells in many of the vessels. A=alveolus, B=bronchiole, V=uninvolved vessel, and TE=tumor emboli. (B) Enlargement of the rectangular inset in A. (Original magnification $\times 600$.)

contain 0.16 per cent of the administered dose per gram. The values are approximate since uniform distribution of the radioactivity can not be assumed. The values obtained from the left lung are not significantly different from those obtained on a patient who died suddenly of cardiac arrest with coronary atherosclerosis 18 hours following an uneventful lung scan. An attempt to determine the histologic location of the radioactivity in the lung using autoradiography was unsuccessful.

DISCUSSION

The macroaggregates of albumin used for lung scanning are bio-degradable. Presumably, particles temporarily occlude the small pulmonary capillaries.^{4,10} The half-time of radioactivity in the lung, which is particle size dependent, is about 6 hours.⁴ Particles which pass through the lung are

phagocytized by the reticuloendothelial system. 12,14

It may be conservatively estimated that 1/200 of the normal vascular bed is temporarily occluded. Estimations from particle counting per unit volume and calculation indicate that there are 250,000 to 1,000,000 macroaggregates per mg. of albumin. The number of particles per mg. will obviously vary with the particle size distribution. Weibel¹⁵ has reported that in the normal lung there are 200 to 300 million pre-capillary segments whose diameters are probably in excess of 10 μ , and, hence, most of the particles might be expected to lodge in these pre-capillaries. The particles between 7 and 10 μ will probably lodge in the more distal and more numerous (280 billion) capillary segments. The estimate of the fraction of the vascular bed occluded is, therefore, 200 million pre-capillary segments divided into the I million particles, or 1/200. The following assumptions were made for this estimate: (1) The minimal number of pre-capillary segments was assumed to be present. (2) It was further assumed that each particle injected occluded one pre-capillary segment. This is not true since about 40-70 per cent of the particles are less than 10 μ (Table II). Those particles greater than 10 may be distributed in such a fashion that 2 or more particles could lodge in the same pre-capillary, thus reducing the total number of capillaries occluded. (3) It was also assumed that there was no collateral blood flow between capillary segments.

In view of these assumptions, a more realistic estimate may be that 1/1,000 of the normal vascular bed is occluded by the injection of 1 million MAA particles for a lung scan. Taplin⁹ has estimated this fraction to be 1/10,000 for a lung scan using 0.2 mg. of albumin.

The degree to which the physiology of the lung is disrupted by this procedure will depend upon the ratio of the available pulmonary capillary bed to the number of capillaries occluded by MAA particles. A disease process may markedly diminish the available pulmonary capillary bed and/or reduce larger vessels to a size which will entrap MAA particles. Under these circumstances, the number of vessels occluded may represent a significant portion of the total pulmonary vasculature.

There is evidence to suggest that the normal lung responds to embolic vascular occlusion by the dilatation of vessels to produce "arteriovenous shunts" within the lung. Such shunts in animals have been shown to pass rather large particles, 100μ . If all such compensatory mechanisms were already operating or were unable to respond further, vascular occlusion could lead to decreased left ventricular output with cardiac and cerebral ischemia and rising right atrial pressure. The events observed in this patient could be explained on the basis of such physiologic changes.

Limited physiologic studies had been done prior to the lung scan and are shown in Table 1. These studies show a loss of lung volume and diffusing capacity. Some of the decrease in lung volume would be anticipated on the basis of the pleural changes in the right lung, but the decrease is probably greater than might have been expected. The decrease in diffusing capacity is out of proportion to the change in lung volume. This could be related to changes in alveolar capillary membrane or a decrease in avail-

able pulmonary capillaries and/or blood flow.

Blood gas studies done following the injection of the MAA are shown in Table III. The very low arterial oxygen tension which later rose is suggestive that a significant degree of venous admixture was occurring in the immediate postinjection period which subsequently decreased. The response to oxygen via face mask does not really permit any calculation of O2 gradients, but one would predict that a significant alveolar to arterial gradient still existed when the PaO2 was only 102 mm. Hg and might be further evidence of the importance of venous admixture. The degree of reduction of diffusing capacity is rather marked, but we have seen reduction in diffusing capacity in patients with multiple pulmonary emboli, though usually not of this degree. Of the 98 other patients studied by lung scan at the University of Michigan, 14 have had concurrent diffusing capacity measurements with values ranging from 45 per cent to 98 per cent of the predicted value.

RADIOPHARMACEUTICAL ASSAY

Two different preparations of MAA have been used for lung scanning. Their pertinent properties are presented in Table II. The MAA given to the case described was

TABLE III
STUDIES FOLLOWING MAA ADMINISTRATION

Gas Value	Predicted	20 min.*	65 min.*		
Gas value	Normal	Room Air	Room Air	Oxygen	
Arterial Oxygen Tension (P _s O ₂)	95+ mm. Hg	38 mm. Hg	52 mm. Hg	102 mm. Hg	
Arterial Oxygen Saturation (S _a O ₂)	>95%	68%	87%	96%	
Arterial Carbon Dioxide Tension (PaCO2)	40 mm. Hg	25 mm. Hg	25 mm. Hg		
pH	7.41	7.48	7.56		

^{*} Time elapsed since injection of MAA.

Product B, but is not included in the composite Product B analysis. One patient was given MAA from the same lot (0.141 mg./ kg.) I day prior to its use in W.M. No clinical reaction was noted and a lung scan and subsequent pulmonary angiogram showed multiple emboli. W. M. received a greater than average albumin dose of Product B, though not the largest dose given in our series of patients (Table II). It has been reported that various healthy animals given single injections containing less than 10 mg. MAA per kg. body weight suffered no detectable changes in pulmonary artery pressure and respiratory rate. 12,14 Rats receiving up to 10 mg. per kg. were indistinguishable from control rats as determined by histologic examination of the lungs immediately and I week after injection.14 Abnormalities in respiratory rate and pulmonary artery pressure have been observed at 20 mg. per kg. It has been cautioned that these data were from normal animals.3 The safety factors thus derived are, therefore, of questionable value when applied to a patient with significant pulmonary vascular embarrassment. If 10 mg. per kg. can be considered to be a physiologically "safe" dose, then in this patient the "safety factor" should have been at least 45.

The hemodynamic tolerance of the MAA as measured by pulmonary artery pressure in the dog appears to be directly related to particle size as well as quantity of albumin.8,12 As the particle size diminishes, the amount of MAA tolerated increases.1 Thus, to achieve maximum tolerance, one should use the smallest particles and the least amount of albumin compatible with an acceptable lung scan. Particles below 7.5 μ in diameter (the diameter of a red blood cell) pass through the pulmonary capillary bed too rapidly to permit lung scanning. A particle size range of 10-50 μ appears to be optimal. Particles above 50 μ are probably of little additional value and increase the risk of a reaction similar to the type observed here.

This patient represents a rather unusual

situation, because of her terminal condition and severe degree of pulmonary vascular occlusion. Certainly, the chances of a reaction could be lessened by avoiding ill patients, but this would negate the value of the lung scan. There were no clinical or laboratory findings unique to this patient with the possible exception of her diffusing capacity measurements, which have not been seen in other patients undergoing lung scan. The combination of particle size, albumin dose and, most importantly, the underlying pathology, gave rise to a high risk situation in the case presented.

FUTURE PRECAUTIONS

Patients with similar suspected pathology possibly should be given the MAA slowly, e.g., 2 minutes, and observed for increasing dyspnea, tachypnea and cyanosis. In order to give the patient less albumin at one injection, one could consider positional injections. It has been suggested that a major portion of the MAA I¹³¹ is deposited in the dependent lung.13 Relatively fewer particles would occlude the nondependent lung. If this observation proves to be true over the spectrum of lung disease, a smaller albumin dose theoretically could be administered. Each lung then could be scanned in turn with a separate injection of MAA I¹³¹ containing one-half the usual dose. This procedure would be cumbersome and is not recommended where small doses of albumin are to be given. On the basis of this experience, it is suggested that a patient should not receive more than 0.020 mg. of albumin per kg. An MAA preparation similar to Product A (Table II) certainly makes such a dose feasible. With these precautions in mind, performance of the lung scan has continued at this hospital.

The minimal amount of albumin compatible with an adequate lung scan has not been determined. It would appear that until such a minimum is found, efforts should be made to produce the highest specific activity MAA I¹³¹ possible, thus reducing the amount of albumin to be given to the patient. A more ideal product than

those available would be one with a specific activity greater than 1 mc/mg. and a particle size range of 10 to 50 μ , with little variation from lot to lot.

SUMMARY

A reaction was observed following the administration of macroaggregated albumin (MAA) for a radionuclide perfusion lung scan in a patient with widespread tumor emboli to the lung. The reaction consisted of faintness, cyanosis, agitation, diaphoresis, tachypnea, a fall in blood pressure and engorged neck veins immediately after intravenous injection of the MAA.

This response suggests that in some patients with pulmonary disease, the safety factor for the MAA lung scan may be decreased and suggestions are presented to minimize the hemodynamic hazards in such individuals.

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NONFATAL AMNIOTIC PULMONARY EMBOLISM*

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AMNIOTIC fluid embolism is frequently fatal. Out of 91 cases reported in the English language literature, Scott⁴ in 1963 was able to find 14 patients who survived. As there have been only 2 reports in the radiologic literature, 1,2 it was thought worthwhile to report the following case of presumptive amniotic pulmonary embolism where characteristic roentgenographic findings were obtained.

REPORT OF A CASE

The patient was a 26 year old woman. The last 3 of her 5 children were delivered by cesarean section. She was admitted on August 9, 1964 at 1:30 A.M. in early labor. At 5:15 A.M., the membranes ruptured and 3 hours later a normal infant was delivered by section under spinal anesthesia; 500 cc. of blood was given during the procedure.

Immediately after the operation, the patient became short of breath and sounded "congested." A few hours later, she vomited twice and coughed up thick yellowish material, slightly blood tinged. She felt cold and her skin was clammy. She appeared to be very apprehensive and her eyes were rolling back; she answered to her name but not to questions. The blood pressure was 100/70 and the pulse rate 134. Bubbling rales could be heard over both lungs as well as a Grade II systolic murmur over the left sternal border. There was no pain or fever.

A bedside chest roentgenogram (Fig. 1) in the afternoon showed an extensive bilateral infiltration of symmetric distribution, fanning out from the hili. The heart was not enlarged and there was no pleural fluid.

She was started on nasal oxygen inhalation, aminophylline and penicillin. Heparin was given at first, but stopped after the possibility of amniotic fluid embolism was suggested.

During the next day she rapidly improved, her dyspnea disappeared and the heart rate returned to normal. Sputum studies revealed no pathogens. All laboratory studies were normal including the fibrinogen level.

A chest roentgenogram (Fig. 2) 2 days later showed no significant change over the first study, but on another roentgenogram (Fig. 3) 2 days later, all pathologic changes had cleared up. She was discharged a few days later, fully recovered.

DISCUSSION

The clinical, laboratory and pathologic findings in amniotic fluid embolism have been fully documented.^{3,4,5} Dyspnea, tachycardia, cyanosis, cough, apprehension and rales in the lungs are the prominent features. Because of defibrinogenation of the blood, excessive hemorrhage may occur. Most cases are seen after prolonged, difficult labor in multiparous women. A few



Fig. 1. Bedside chest roentgenogram 6 hours after delivery. Massive pulmonary infiltration.

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cases have been reported after cesarean sections as in the present case.

Pathologically, amniotic fluid components can be demonstrated in the pulmonary arterioles and capillaries. Squamae, mucin and lanugo particles have been found. The obstruction of pulmonary capillaries leads to edema.

In the presented case, extensive edematous changes were seen on a chest roent-genogram 6 hours after delivery. These were most pronounced in the more central portions and were equally present on both sides. After 4 days no residual remained. In the case reported by Arnold *et al.*, the infiltration took more than 20 days to clear up; in Cornell's² case complete clearing had occurred after about 3 days. Scott reported resolution after 5 days.

SUMMARY

A case of nonfatal amniotic fluid embolism is reported where the diagnosis was

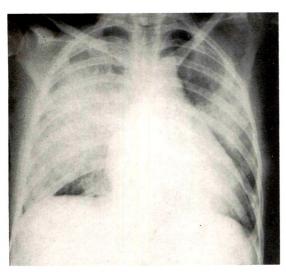


Fig. 2. Bedside chest roentgenogram 2 days later. Clinically, the patient had improved markedly.

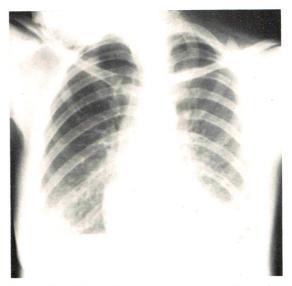


Fig. 3. Bedside chest roentgenogram 4 days after first study. Complete resolution of the infiltration.

made on a clinical and roentgenographic basis.

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LYMPHOGRAPHY IN A PATIENT WITH NONREACTIVE TUBERCULOSIS*

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LYMPHOGRAPHY has in recent years become an additional procedure for the diagnosis of malignant diseases. Rarely, however, has it been used for the detection of inflammatory processes. In the present paper, the clinical, pathologic and lymphographic findings of a case of nonreactive tuberculosis (typhobacillosis of Landouzy) are reported.

REPORT OF A CASE

The patient was a 45 year old unmarried white female, admitted to the Medical Clinic of Geneva on April 17, 1965 with the chief complaints of anorexia, asthenia and rapidly progressing ascites. The first signs dated back to the summer of 1964 when the patient noticed vague epigastric pain and swelling of the abdomen. In November, 1964, she was treated with topical cortisone in the Ophthalmologic Clinic for a left optic neuritis. In January 1965, she consulted her physician for anorexia, asthenia and a markedly distended abdomen.

Her previous history was of no significance except for an incompletely documented pleuro-pneumopathy at the age of 20 years. No history of tuberculosis in the members of her family or any contact with a tuberculous milieu could be elicited.

On admission, the patient was markedly asthenic and anorexic but in no acute distress. Minimal exercise was accompanied by dyspnea and dry cough.

Physical examination revealed a temperature of 37.7° C., pulse rate of 105/min., and a blood pressure of 105/80 mm. Hg. The patient weighed 55 kg. and her height measured 165 cm. Her distended abdomen with a network of dilated superficial veins contrasted strikingly to her general emaciated appearance. The abdominal circumference at the level of the umbilicus was 84 cm. Cardiac auscultation revealed a pericardiac friction rub. Examination of the chest indicated signs of light bilateral pleural effusion.

Admitting diagnosis was polyserositis of either hepatic, carcinomatous or tuberculous origin.

The major laboratory findings were as follows: sedimentation 5 mm. after 1 hour; red blood cells, 3,600,000; leukocytes 3,200 with a shift to the left. The blood chemistry revealed a normal electrolyte balance, decreased total proteins and slightly increased transaminase and alkaline phosphatase. The hepatic function tests were altered. Urinalysis and stool were normal. The purified protein derivative reaction with 3 IU was negative.

Pleural and peritoneal taps yielded a pseudochylous protein-rich liquid which revealed acidfast bacilli of human type, sensitive to the usual antituberculous drugs.

A chest roentgenogram demonstrated 2 non-homogeneous nodular opacities in the basal segments of each lung which were interpreted as old, nonactive lesions. There was a slight bilateral pleural effusion (Fig. 1).

In an attempt to establish a correct diagnosis in a relatively brief period, lymphography was performed on April 22 for the purpose of excluding a malignant lesion. The technique consisted of marking the lymphatics of the foot by patent violet blue, dissection, cannulation and

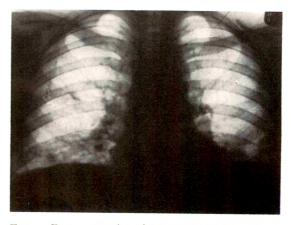


Fig. 1. Posteroanterior chest roentgenogram showing slight pleural effusion and small basal opacities.

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slow injection of 10 cc. of lipiodol ultra-fluid bilaterally over a period of 2 hours. Roentgenograms of the pelvis and thorax were made immediately after completion of the injection and again 24 hours later.

The contrast medium reached the thoracic duct in normal time (Fig. 2) despite peripheral lymphatic stasis. The inguinal and iliac lymph nodes seemed to be normal. The lumbar lymph nodes were enlarged and inadequately opacified; their borders were ill-defined. At this level the lymphatic tissue normally undergoing strong opacification was practically absent. Instead, delicate lymph vessels coursing around the totally replaced lymph nodes and small areas of remaining lymphatic tissue were visualized (Fig. 3 and 4). No definite diagnosis was made at this examination.

The course of the disease was rapidly downhill, despite energetic antituberculous treatment with streptomycine, isoniazid, PAS, trecator and prednisone. The patient developed electrolyte imbalance with paralytic ileus, jaundice and a secondary urinary infection. She

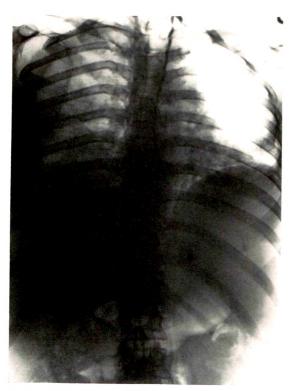


Fig. 2. Chest lymphogram made just after the injection of contrast medium showing an opacified patent thoracic duct.

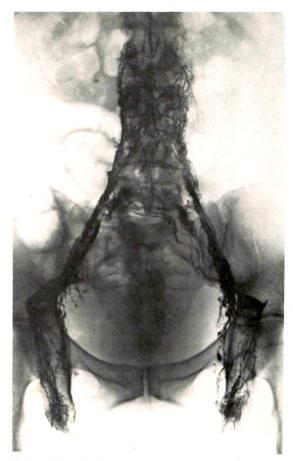


Fig. 3. Lymphogram made just after the injection of contrast medium showing significant dilatation of the lymphatic channels at the lumbar level.

died on May 22, 1965, one month after her hospitalization.

Autopsy Findings. Postmortem examination revealed the presence of a nonreactive tuberculosis, the progress of which was not slowed by any immunologic mechanism. This was manifested by a tuberculous peritonitis with 7,000 cc. of hemorrhagic ascites, and massive necrosis of the lymphatic ganglia and retroperitoneal soft tissues. Branches of the portal vein were thrombosed secondary to a tuberculous phlebitis which had destroyed the liver parenchyma extensively. The pancreas was grossly damaged. The spleen showed large areas of necrosis and sinusoidal thromboses. The lungs were the site of a caseous bronchopneumonia without tubercle formation. Other postmortem findings were: advanced myocardosis (180 gm.), osmotic nephrosis, and a meningioma located at the optic chiasma compressing the left optic nerve.

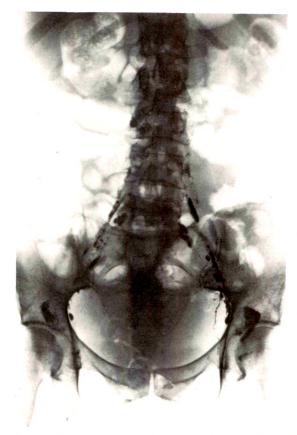




Fig. 5. Postmortem roentgenogram of the paraaortic and para-iliac lymph node chains (see text).

Fig. 4. Lymphogram made 24 hours after the injection of contrast medium (see text).

The aortic, iliac and mesenteric lymph nodes were involved in a massive necrotic process. Their usual texture was completely destroyed and their capsules were hardly visible. Their parenchyma was substituted by glistening or finely granular necrotic areas. Only a few isolated islands of lymphocytes remained. The surrounding adipose tissue was also involved in the necrotic process. The extent and confluence of the necrosis erased the demarcation line between lymphoid and adipose tissue. Ziehl preparations showed colonies of acid-fast bacilli in the necrotic areas. A few intact lymph nodes showed dilated lymphatic channels, some with deposit of contrast medium (Fig. 5).

Scattered throughout the adipose tissue in the areas of the affected lymph nodes were islands of newly formed lymphoid tissue. A tendency of the tissue to undergo sclerosis was evidenced by a pale red coloration on van Gieson's stain. No tubercle formation nor any giant or epitheloid cells were seen (Fig. 6).

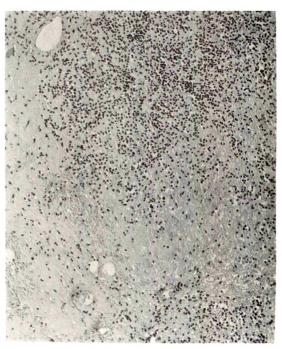


Fig. 6. Para-aortic lymph nodes showing loss of structure with necrosis extending into soft tissue (hematoxilin-eosin, 96×).

DISCUSSION

The reported case is an example of the tuberculous process described by Landouzy as typhobacillosis. In such instances, the natural organic defenses are completely lacking, as evidenced in this patient by a normal sedimentation rate and a negative purified protein derivative reaction in the presence of acid-fast bacilli in the exudates. The tissue energy was shown at postmortem examination by the absence of epithelioid and giant cells, presence of massive necrosis in the reticuloendothelial system and finally, by minor involvement of the lungs.

No serologic or histologic explanation for this anergy was found; in particular no signs of hemopathy were observed, as were previously reported in such cases.

The lymphographic pattern correlates well with the histologic aspect of the lymph nodes. These pathologic changes may be seen in a later stage of tuberculosis determined by fibrosis and hyalinization. Similar lymphographic patterns are observed in the fibrotic stage of Hodgkin's disease, save perhaps the extent of the process. Differentiation based upon roentgenologic grounds may be impossible.

SUMMARY

The clinical, roentgenologic and histologic aspects of nonreactive tuberculosis are presented. The lymphographic pattern is

very similar to that seen in the advanced stage of Hodgkin's disease and constitutes an interesting criterion in differential diagnosis.

In our case, the pathologic findings did not explain why the organism failed to respond to the tuberculous aggression.

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SUPERIOR VENA CAVAL SYNDROME DUE TO TUBERCULOSIS*

REPORT OF THREE CASES

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CUPERIOR vena caval obstruction due o to tuberculosis and causing the superior vena caval syndrome²¹ is apparently uncommon. Aufses and Neuhof, in 1948, reported a case which is also included in this paper and found references to 48 others in the world literature. Recently, Urschel and Paulson²² published a patient with superior vena caval syndrome in a series of 61 cases. Several authors have operated on mediastinal masses which proved to be tuberculomas^{7,12,19,22} and granulomas.¹⁰ None of these, however, involved the superior vena cava and this was also true of the 48 cases of tuberculoma found among 782 cases of mediastinal tumors in military personnel published by Lyons and co-workers.¹² Idiopathic mediastinal fibrosis, on the other hand, although rare, commonly occludes the superior vena cava.2,8,5,8,14,21 Although, in recent times, histoplasmosis has been incriminated, 11,18,16,17 cancer of the lung has become the most common cause of the superior vena caval syndrome.4,16,16,19,20 The diagnosis of the vena caval obstruction of tuberculous etiology is, therefore, important because effective drugs are available for treatment of the disease. It is for this reason that 3 adult women, 2 of whom had exploratory thoracotomies, are reported.

REPORT OF CASES

CASE I. Superior vena caval occlusion due to tuberculous mediastinitis. A 39 year old Caucasian woman, complaining of swelling of the face, neck, and arms, and a bursting sensation in the head and temples, was seen in this center on March 19, 1948. Because of these symptoms and following venograms which showed supe-

rior vena caval and left subclavian vein occlusions, she had had an exploratory thoracotomy at Mount Sinai Hospital on June 2, 1944. Her case was fully reported by Aufses and Neuhofin 1948. A firm, diffusely infiltrating mass occupying the entire mediastinum was found, but only liberal biopsy specimens were excised. These showed chronic fibrosing tuberculous mediastinitis. Before discharge from Mount Sinai Hospital on June 23, 1944, another bilateral venographic study failed to show improvement of the venous occlusions. The venous pressures in both arms were also elevated.

In 1948, at this center, she still complained of bursting sensations in the temples and swelling of the face, neck, and chest. Her weight was 145½ pounds and her height was 62 inches. A roentgenogram of the chest showed a widened mediastinum and flattening of the left diaphragm. The face, neck, and upper thorax were plethoric and contained prominent veins. Four years later, because of wheezing, easy fatigability, dizziness and faintness, streptomycin and paraaminosalicylic acid were prescribed and her tiredness decreased. In 1956, her weight increased to 152 pounds. She still felt dizzy on bending and exertion, and with excessive laughter she became faint. Isoniazid was added to the anti-tuberculosis treatment regimen because of a small, left infraclavicular infiltrate (Fig. 1). The patient was last seen on April 27, 1966, because of sudden onset of stridor and respiratory distress during the night. Physical examination showed her to be obese with well developed collateral circulation of the neck and upper thorax. Respiratory distress and stridor recurred when she was placed in the supine position and was alleviated when the head was elevated. The roentgenogram of the chest was unchanged compared to Figure 1.

CASE II. Partial occlusion of the superior vena cava cured by surgical resections of tuberculous

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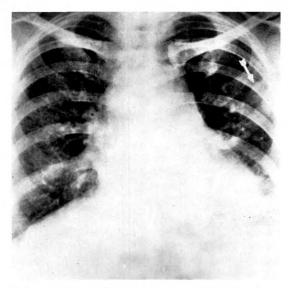


Fig. 1. Case 1. Frontal teleroentgenogram of the chest made in 1956, 12 years following thoracotomy. The mediastinum is widened and there is a small left infraclavicular infiltrate (arrow).

lymph nodes. A 50 year old Caucasian housewife (N.Y.H. No. 828412), referred by Dr. Cranston W. Holman, was admitted on July 9, 1959, with complaint of pressure in the neck of 3 months' duration. The patient had always been well until she stooped to pick up an object and felt fullness of the neck. She had no difficulty in swallowing or breathing. The neck pressure recurred whenever she bent over and so she consulted her doctor who referred her to a thyroid specialist who, however, found no abnormalities. Six weeks prior to admission, tightness in the neck began, especially when in the supine position. For relief she began sleeping on 2 pillows. She denied cough, expectoration, hemoptysis, or contact with patients with tuberculosis.

On physical examination, the patient was well developed and well nourished, weighing 130 pounds, height 62 inches. The neck was supple, the veins were distended, but no masses were felt. The chest was clear and resonant. The heart was normal in size. No murmurs were elicited, and the blood pressure was 140/80 mm. Hg in both arms. There was no edema of the legs and the liver was not palpable. Roentgenograms of the chest showed a small nodular mass containing calcium located in the right superior middle mediastinum and hilus (Fig. 2, A, B and C). An angiocardiogram demonstrated a markedly narrowed superior vena cava with dilated subclavian and jugular veins (Fig. 2D).

Scalene biopsy on July 10, 1959, and bronchoscopy on July 14, 1959, yielded normal lymph node and bronchial tissues. A sputum specimen failed to show tumor cells. Accordingly, an exploratory thoracotomy was performed by Dr. Cranston W. Holman on July 17, 1959. A mass just above the azygos vein encircled the trachea and superior vena cava and grossly had the appearance of a neoplasm. Several biopsies proved to be negative for tumor; further dissection finally revealed that the mass consisted of caseous lymph nodes. Not all of the tissue could be excised because of adherence to the superior vena cava and trachea. Another caseous mass was found at the right hilus (Fig. 2C) and partially removed. Palpation of the entire right lung revealed no disease. Histologic studies of the excised specimen showed eosinophilic caseous-like necrotic material, fibro-collagenous bundles, and chronic inflammatory cells (plasma and lymphocytes) of healed tuberculosis of the bronchial lymph nodes. Smears and cultures of the caseous material from the lymph nodes were negative for the tubercle bacillus. The patient had an uneventful convalescence. She was treated with isoniazid and discharged on the twelfth day following operation, the symptoms of pressure in the neck having been alleviated. Recent communication with her physician disclosed that after 18 months isoniazid therapy was stopped and that she has continued to be in good health.

CASE III. Occlusion of the superior vena cava with well established azygos-inferior vena caval collaterals. A 57 year old Caucasian housewife (N.Y.H. No. 716865) was admitted on December 10, 1964, with a complaint of shortness of breath of 1 year's duration. This had gradually increased, became paroxysmal at night, and edema of the legs developed. She was treated with bed rest, digitalis, and diuretics but did not improve although she lost 12 pounds in weight. Firally, she was referred to a member of our staff who noted that the patient had intermittent cyanosis of the lips and fingertips, plethora, and dyspnea in the supine position.

Physical examination revealed a well developed and well nourished woman weighing 122 pounds, height 64 inches. The face was ruddy and the neck veins were distended. The venous pressure was 160 mm. (saline) at the angle of Louis. The lungs were clear, the heart was not enlarged, and there were no murmurs;

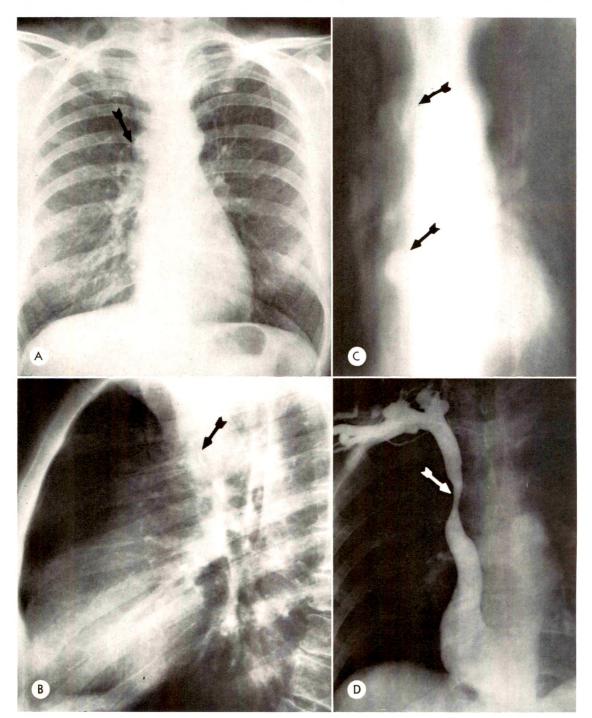


Fig. 2. Case II. (A) Frontal teleroentgenogram of the chest showing a small, partially calcified, 2×2 cm. mass in the right paratracheal area (arrow). (B) Lateral roentgenogram showing the middle mediastinal location of the partially calcified mass (arrow). (C) Laminagram showing the paratracheal mass (upper arrow) and another one at the right hilus (lower arrow). (D) Frontal angiocardiogram showing the markedly narrowed superior vena cava (arrow). Note the dilated subclavian and jugular venous channels above.

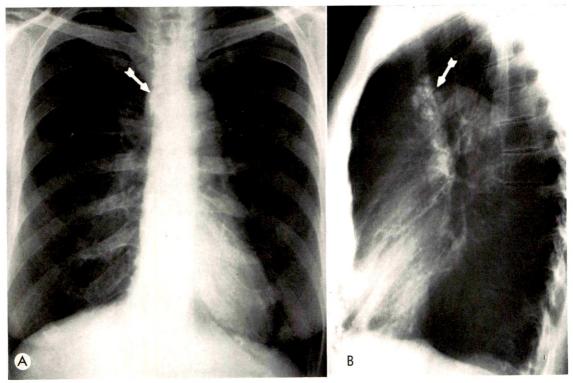


Fig. 3. Case III. (A) Frontal teleroentgenogram of the chest showing the partially calcified 2×3 cm. mass in the right superior mediastinum (arrow). (B) Lateral roentgenogram shows the partially calcified superior middle mediastinum mass to advantage (arrow).

the blood pressure was 150/100 mm. Hg. The liver was enlarged 4 cm. below the right costal margin. The electrocardiogram showed a right ventricular conduction defect, ST and T wave abnormalities, and regular rate of 70 per minute. Roentgenograms of the chest revealed a normal-sized heart and small calcified right superior middle mediastinal and hilar masses (Fig. 3, A and B). Intravenous angiocardiograms showed occlusion of the superior vena cava with immediate filling of the azygos vein and opacification of the inferior vena cava (Fig. 3, C, D and E). The right atrium, ventricle, and pulmonary artery were normal in size (Fig. 3, E and F). Since the venous collateral channels seemed adequate and the patient was improved, she was discharged after a stay of 6 days. Anti-tuberculosis treatment did not seem indicated and was not prescribed.

The patient was readmitted to the hospital on January 5, 1966, because of recurrence of dyspnea. The tuberculin (intermediate strength) test was positive; the histoplasmin skin test was negative.

DISCUSSION

Superior vena caval occlusion in adults is an ominous sign most commonly due to carcinomatous involvement.4,16,19,20 For this reason, every effort should be made to establish the definitive diagnosis. In order to rule out carcinoma of the lung, sputum cellular studies, bronchoscopic examination and scalene node biopsies are indicated. When these fail to establish the diagnosis, exploratory thoracotomy is justified. 1,2,10,18,22 In 2 of the 3 patients herein reported, thoracotomy established the diagnosis of tuberculosis as the cause of the superior vena caval occlusion (Case 1 and II). In a third patient (Case III), calcified tissue in the region of the superior vena cava suggested that tuberculosis was the cause of the superior vena caval syndrome. Because histoplasmosis may also produce a similar lesion, 6,9,13 the etiologic diagnosis was not established with certainty. How-

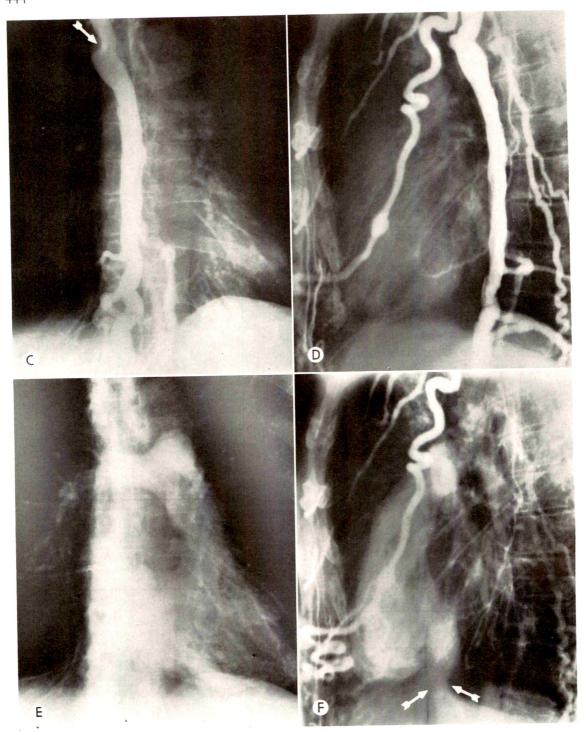


Fig. 3. (C) Frontal angiocardiogram showing occlusion of the superior vena cava with immediate opacification of the azygos system (arrow). (D) Lateral (biplane) view of C. Note the marked azygos collaterals. (E) Frontal angiocardiogram at a later time showing opacification of the inferior vena cava, right atrium, ventricle, and pulmonary artery. (F) Lateral (biplane) view of E. Arrows point to the opacified inferior vena cava filled in retrograde fashion from the azygos system.

ever, whether the superior vena caval occlusion is due to tuberculosis or histoplasmosis is of academic interest because the well established azygos-inferior vena caval collaterals made surgery unnecessary. Sleeping in the Fowler position afforded relief and this therapy was recommended on discharge from the hospital.

SUMMARY AND CONCLUSIONS

Three middle-aged women with swelling of the face, neck, and arms—characteristic features of the superior vena caval syndrome—were found to have superior middle mediastinal masses. Exploratory thoracotomy revealed tuberculous mediastinitis occluding the vena cava in the first case. In the second patient, the superior vena cava was markedly narrowed by middle mediastinal caseous bronchial lymph nodes. In the last patient, a calcified mass in the superior middle mediastinum occluded the superior vena cava. The azygos and hemiazygos systems, however, very efficiently filled the heart via the inferior vena cava. Sleeping with the head of the bed elevated alleviated her symptoms and so surgery was not indicated. Although histoplasmosis was not ruled out in the last case, it would appear that mediastinal tuberculosis or histoplasmosis rather than pulmonary cancer or lymphoma may, in rare instances, produce the superior vena caval syndrome in middle age, and, therefore, these diseases should be considered in the differential diagnosis.

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SUBCLAVIAN AND INTERNAL MAMMARY ANGIOGRAPHY IN THE EVALUATION OF ANTERIOR MEDIASTINAL MASSES*

By ERIK BOIJSEN, M.D.,† and STEWART R. REUTER, M.D.,‡

THE common anterior mediastinal masses include thymomas, teratomas and dermoid cysts, lymph node enlargements, aneurysms, substernal thyroids, and metastatic tumors. Some of these lesions can be differentiated by ordinary roentgen diagnostic methods or angiocardiography, but a definitive diagnosis usually cannot be made. To investigate the role of selective angiography in the diagnosis of anterior mediastinal masses, we have reviewed the subclavian and internal mammary angiograms which have been made at the Roentgendiagnostic Department, University of Lund.

MATERIAL AND METHOD

Twenty-two patients have been examined because of anterior mediastinal masses with either selective subclavian or internal mammary angiography. Histologic verification was obtained in 17 of these. This group of proven cases comprises the material of this report. Seven of the masses were thymomas, 5 were metastases, 2 were substernal thyroids, 2 were dermoid cysts, and I was lymphadenopathy secondary to sarcoidosis.

Angiography was performed by the percutaneous approach. Usually, an attempt was first made to enter the internal mammary artery selectively. If this was not successful, or if no blood supply to the tumor was demonstrated, the catheter tip was placed in the subclavian artery near the internal mammary orifice for the injection. Internal mammary injections were made by hand using 10 cc. of 60 per cent

urografin (Schering, Germany), and subclavian angiographies with a pressure injector using 20 cc. of the medium.

RESULTS

In each case of thymoma, the tumor was supplied by a dilated thymic artery arising from the internal mammary artery 4 to 5 cm. distal to its origin (Fig. 1, A and B). In upper mediastinal thymomas, it was the only branch from the internal mammary artery to the tumor. In 2 of the thymomas which extended into the lower mediastinum, branches also arose from the lower part of the internal mammary artery to supply the lower part of the tumor. The thymic artery could be displaced either anteriorly, laterally, or posteriorly by the tumor. These lesions were moderately vascular, and a few tumor vessels were observed. In 3 of the thymomas which extended across the mid-line, the vascular supply of the tumor on the side opposite the injection was not demonstrated. Presumably, this blood supply came from the opposite thymic artery.

The metastatic tumors consisted of I thyroid and 3 bronchogenic carcinomas which had invaded the anterior mediastinum directly, and I squamous cell carcinoma of unknown origin. In 4 of the 5 lesions, many small internal mammary artery branches dilated slightly to supply scattered, localized areas of the tumor (Fig. 2, A and B). No displacement or invasion of major vessels was noted, and the accumulation of contrast material was markedly uneven. No veins were observed. One of the broncho-

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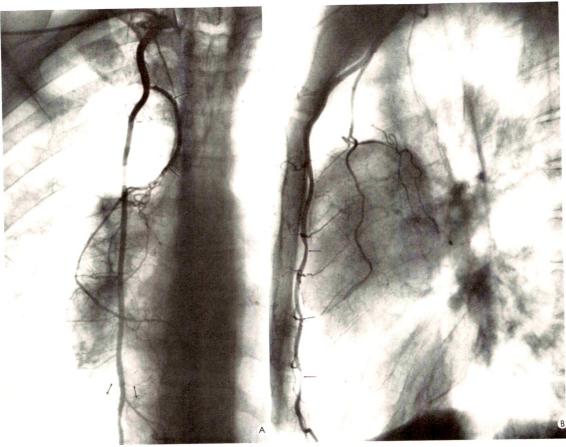


Fig. 1. Thymoma. Internal mammary angiography. (A) Anteroposterior projection. The dilated thymic artery (\rightarrow) supplies a moderate number of tumor vessels throughout the mass. Small branches of the distal internal mammary artery (\rightarrow) supply the lower part of the tumor. (B) Lateral projection. The tumor compresses the internal mammary artery as it passes over the posterior surface of the costal cartilages (\rightarrow) .

genic carcinomas was partly supplied by the thymic artery. Unlike the thymomas, however, many tumor vessels were present in these tumors.

In the patients with *dermoid cysts*, the branches of the internal mammary artery which supplied the masses were not dilated, but were stretched and displaced (Fig. 3, A and B). No accumulation of contrast medium or tumor vessels was seen. In both cysts, the thymic artery participated in the blood supply. It was displaced but not dilated.

In the 2 patients with *substernal thyroids*, the entire blood supply to the mass came from a markedly dilated inferior thyroid artery. The masses were very vascular, with many small, irregular vessels, uneven

and dense contrast accumulation, and early venous filling (Fig. 4).

In the patient with *sarcoidosis*, several small internal mammary artery branches supplied the enlarged lymph nodes. The mass was hypervascular, and small, irregular vessels were seen within it. No accumulation of contrast medium or venous filling was observed.

DISCUSSION

Some of the lesions in this series had angiographic features which may be useful in the differentiation of anterior mediastinal masses. If the blood supply comes primarily or exclusively from a dilated thymic artery, the tumor is probably a thymoma. The thymic artery, however,

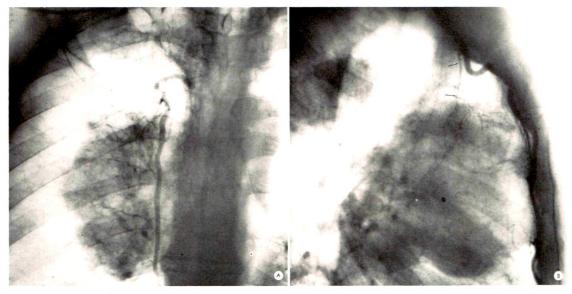


Fig. 2. Metastasis from a bronchogenic carcinoma. Internal mammary angiography. (A) Anteroposterior projection. Branches of the mid-internal mammary artery supply small, localized areas of the tumor. (B) Lateral projection. Part of the blood supply comes from the thymic artery (\rightarrow) . The major part of the blood supply is from the bronchial circulation (demonstrated at selective bronchial angiography).

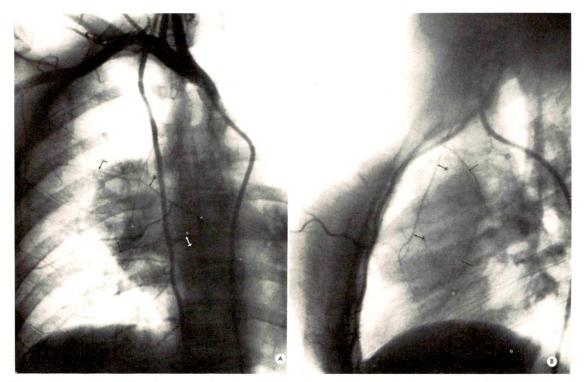


Fig. 3. Dermoid cyst. Subclavian angiography. (A) Anteroposterior projection. Normal sized branches of the internal mammary artery are displaced and stretched by the mass. No tumor vessels are seen. The vessel crossing the mass is an internal mammary branch to the breast (→). (B) Lateral projection. The thymic artery (→) is displaced posteriorly by the mass. The long thoracic artery (→) is projected over the mass in this projection.



Fig. 4. Substernal thyroid. Subclavian anteroposterior projection. A dilated inferior thyroid artery supplies the markedly vascular mass.

also participated in the blood supply of a malignant tumor which invaded the thymus. Metastatic tumors have blood supply from several branches of the internal mammary artery, and the accumulation of contrast medium in the tumor varies markedly from area to area. An avascular mass supplied by a normal number of vessels, which are displaced by the mass, probably is a dermoid cyst.

To be absolutely certain that the entire blood supply to an anterior mediastinal tumor is demonstrated, both internal mammary arteries must be injected. In most of our patients, however, the masses did not extend over the mid-line, and adequate information was obtained by injecting the artery on the side of the lesion.

The angiographic findings are not specific in anterior mediastinal tumors. The value of angiography is often not in the determination of a diagnosis, but rather in the confirmation of a tumor's presence and the definition of its extent and blood supply. Moreover, demonstration of the blood supply can sometimes reveal the organ from which the tumor has arisen. Substernal thyroids, for example, receive their blood supply from the inferior thyroid artery. Other roentgen methods can only demonstrate the presence of an anterior mediastinal mass and in some instances define its extent. Direct methods, mediastinoscopy and needle biopsy may reveal the diagnosis, but even these methods may give inconclusive information. Two patients had to be excluded from this series because an inadequate specimen was obtained at needle biopsy. Both patients had angiographic findings suggesting thymoma.

Thoracic aortography and angiocardiography are important methods for differentiating aneurysms from mediastinal tumors.2 The concentration of the contrast medium in the mediastinal vessels with these methods, however, is seldom adequate for definition of the blood supply of a

tumor in the mediastinum.

SUMMARY

The angiographic findings in 17 patients with anterior mediastinal tumors suggest that angiography has a role in the preoperative evaluation of these masses. It should be used if the diagnosis is not apparent at ordinary roentgen examination or if needle biopsy is not successful.

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PNEUMOMEDIASTINOGRAPHY*

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THE study of the mediastinum by conventional roentgenography is limited because the component tissues have similar densities. The internal lumen of the various vascular structures of the mediastinum may be demonstrated by the techniques of venography, angiocardiography, aortography and intraosseous venography, and these methods have all been employed in the investigation of mediastinal pathology. The lumen of the esophagus may be outlined by barium sulfate paste and the trachea and bronchi may be studied by the techniques of tomography and bronchography.

Condorelli developed 2 methods for the demonstration of the mediastinal structures by the injection of gas into the mediastinum; the retrosternal technique⁴ and the transtracheal approach.⁵

METHOD TRANSTRACHEAL

Straight roentgenograms of the chest and thoracic inlet are made to ensure that there is no untoward compression or deviation of the trachea. The patient is fasted before the examination and sedated with a short acting barbiturate (cyclobarbitone 100-200 mg.) together with atropine sulfate 0.6 mg. intramuscularly. The neck is hyperextended over a pillow and the skin and subcutaneous tissues either just above or below the thyroid isthmus, are infiltrated with I per cent lignocaine solution. The lower route just below the thyroid isthmus is preferred, but if there is a prominent aortic arch the higher route above the thyroid isthmus is used. Infiltration is continued down to the trachea and the needle is advanced between 2 tracheal rings into the

lumen of the trachea. Two cubic centimeters lignocaine solution are then injected into the trachea. The patient will cough at this stage, indicating the correct positioning of the needle. The needle is withdrawn and a child's lumbar puncture needle (size 21) is inserted along the same route into the trachea. The needle is then further advanced until resistance to continuous aspiration proves that the point of the needle has just passed through the posterior tracheal wall. Gas is then injected in aliquots of 50 cc., drawn into a syringe from a cylinder through a three-way tap. Aspiration before injection ensures that the needle has not entered a blood vessel inadvertently. Nitrous oxide is employed for the first 100 cc., and if dissection by the gas proceeds normally, this is followed by 200-400 cc. of oxygen. Nitrous oxide or carbon dioxide used alone is absorbed too rapidly and if further roentgenograms are required most of the gas may have been absorbed. The progress of the examination is checked by frequent fluoroscopic control—using a Philips television 9 inch intensifier system. During the induction, the patient experiences some slight discomfort of the chest and on auscultation characteristic crepitations may be heard. No changes have been observed in the electrocardiogram, pulse rate or blood pressure taken at intervals during the insufflation. A satisfactory examination is indicated by the separation of the mediastinal pleura from the pericardial sac down to the level of the diaphragm. Linear tomograms are taken in lateral and anteroposterior projections. In a patient of 60 kg. the exposure factors would be 75 kv. and 100 mas. for anteroposterior roentgenograms and 90 kv. and 160 mas. for lateral

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roentgenograms. When the thymus is to be delineated, less exposure is required: 72 kv. and 100 mas. for the anteroposterior tomograms and 75 kv. and 100 mas. for the lateral tomograms. Following the examination, the patient is confined to bed for 6 hours.

In this method, there is good filling of both the anterior and posterior compartments of the mediastinum and the patient experiences little discomfort.

RETROSTERNAL

In some patients the transtracheal method was contraindicated because of thyroid enlargement sometimes with tracheal deviation or compression. In these cases the retrosternal method was used. A fine curved needle (size 20) is inserted percutaneously through the suprasternal notch so as to just enter the anterior mediastinum behind the manubrium. Injection of the gas will lead to good filling of the anterior mediastinum but filling of the posterior mediastinum is less satisfactory. Discomfort is minimized by introducing the gas into the anterior mediastinum slowly. In the retrosternal method there is theoretically a greater risk of encountering a vascular structure but in our experience this complication has not occurred.

Using the above techniques, pneumomediastinography by either the transtracheal or retrosternal method has not been followed by any morbidity. Stringent precautions were taken against the possibility of gas embolism. The examination must not be undertaken if there is any evidence of upper respiratory tract infection and full asepsis must be maintained. The examination is contraindicated in patients with a bleeding diathesis. With careful positioning, the esophagus should not be punctured during the retrotracheal method. This may have occurred on one occasion in the present series but with no ill effect.

CLINICAL OBSERVATIONS

The examination of pneumomediastinography has been carried out in 110 patients

suffering from a variety of conditions. For the present paper, a number of cases of particular interest has been selected in order to illustrate and discuss the application of this technique.

NORMAL APPEARANCES

The appearance of the "normal" mediastinum as studied by pneumomediastinography is shown in Figures 1 and 2.

In the anteroposterior view, the gas outlines the left innominate vein and the superior vena cava, which tends to move to the right. The azygos vein may be seen in the right tracheobronchial angle. The aorta, innominate artery, left carotid artery and left subclavian artery can readily be demonstrated in a series of anteroposterior



Fig. 1. Anteroposterior tomogram showing normal anatomy. Gas has outlined the aorta, main pulmonary artery, ligamentum arteriosum, azygos vein, left subclavian artery and superior vena cava. Gas also diffused around the trachea and main bronchi, outlining their walls.



Fig. 2. Lateral tomogram showing the two lobes of the thymus outlined by gas in the anterior mediastinum. The trachea, esophagus, left innominate vein and superior vena cava are also seen. Gas has diffused between the right ventricular outflow tract and the aorta.

tomograms. When sufficient gas has been injected into a patient with a normal mediastinum, dissection will occur around the main pulmonary artery and aortic arch, outlining the aortic window (Fig. 1). The outer walls of the trachea and bronchi can be outlined as far as the primary divisions and in many cases the ligamentum arteriosum can be identified. The thymus may be distinguished in the appropriate anteroposterior tomogram as 2 thin shadows on either side of the mid-line. The right lobe of the thymus is closely related to the superior vena cava.

The lateral tomograms following the insufflation of gas are particularly suitable for outlining the thymus. The 2 lobes of what is considered to be a normal thymus are demonstrated in Figure 2. The thymus

may be seen roentgenologically to extend a variable distance inferiorly in the anterior mediastinum. Also, in the lateral tomograms the left atrial wall may be clearly visualized and the external surface of the esophagus may be demonstrated.

During pneumomediastinography, the gas diffuses into the neck and anteroposterior tomograms will clearly delineate the lobes of the thyroid gland (Fig. 3).

DISORDERS OF THE THYMUS

An assessment of the size of the thymus can be made by measuring with the aid of a planimeter the area of the thymic shadow in the sagittal tomogram. Three examples of thymic disorder are described below.

Case I. J.B. This 56 year old woman presented with non-goitrous idiopathic primary hypothyroidism. The clinical diagnosis was confirmed by a low serum level of protein bound



Fig. 3. Anteroposterior tomogram of the cervical region shows the two lobes of the thyroid gland outlined by gas immediately below the larynx.



Fig. 4. Case I. Lateral tomogram. Moderately enlarged thymus in a patient with primary hypothyroidism and whose serum contained thyroid antibodies.

iodine (P.B.I. = 1.5 μ g. per cent) and a low thy roid gland uptake of I³¹ following an oral dose of 20 μ c (48 hr. uptake = 0.9 per cent). Pneumomediastinography was performed after 4 months replacement treatment with thyroxine, 0.2 mg. per day. The thymus is considered to be diffusely enlarged with a cross-sectional area in the sagittal tomogram of 13 cm.² (Fig. 4). At the time of the roentgenographic examination, the patient's serum contained antibody to thyroglobulin in a titer of 1:250 using the tanned cell hemagglutination technique.⁶

A possible relationship between roentgenologic evidence of hyperplasia of the thymus in patients with thyroid disease associated with auto-immunity has been the subject of a separate paper. It was observed that abnormally large thymic shadows were a common occurrence in patients with thyroid disease and who had organspecific antibodies demonstrable in the serum.

CASE II. W.B. A lumberjack, aged 53 years, suddenly developed the symptoms of myasthenia gravis. The classic clinical picture was confirmed by the dramatic improvement following the administration of anticholinesterase. Conventional chest roentgenograms showed no abnormality. After a 3 week period of stabilization with neostigmine, pneumomediastinography was performed and a grossly enlarged thymus was demonstrated (Fig. 5). The crosssectional area of the thymus shadow in the sagittal tomogram was 40.3 cm.2 and the shape of the shadow indicated the presence of a thymoma. Thymectomy was performed 6 weeks later and a large cystic thymoma was removed (Fig. 6). The cyst contained 35 ml. of fluid. The patient made a good recovery and for a period of some months his requirement for neostigmine was low, but subsequently large doses were again necessary to control his myasthenia.

This case illustrates that conventional chest roentgenograms may not always



Fig. 5. Case II. Lateral tomogram. Myasthenia gravis of recent onset. Gas has outlined a clearly defined large mass lying immediately in front of and to the side of the aorta in the anterior mediastinum.

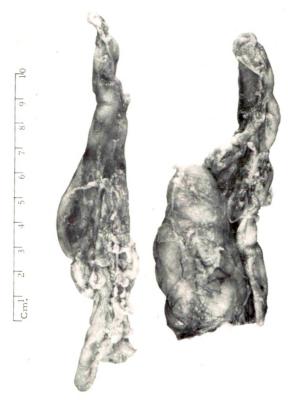


FIG. 6. Case II. Operative specimen (cut longitudinally into 2 parts). The thymus is considerably enlarged due to the presence of a large cyst, the wall of which contained thymoma tissue.

demonstrate thymic enlargement even when this takes the form of a thymoma of considerable size. The thymoma was readily demonstrated at pneumomediastinography.

Case III. C.B. This 26 year old woman presented with an 8 month history of a dry irritating cough and breathlessness on severe exertion. A conventional roentgenogram of the chest showed a mass in the superior mediastinum and the possibility of an aortic aneurysm was considered by the referring physician. A scintigram (I¹³¹) showed a normal distribution of thyroid tissue. Pneumomediastinography using the retrosternal method showed that there was a large lobulated mass lying in the anterior mediastinum closely applied to the aorta and in close relationship to the pulmonary artery. Gas failed to separate the mass from the aorta (Fig. 7 and 8). The mass extended across the mid-line as far as the right border of the sternum. There was no evidence of thymic tissue apart from the mass and it was, therefore, concluded that the mass was either a tumor or cyst arising from the thymus or that the thymus was the site of some other pathology, e.g., reticulosis. There was no evidence of any other mass or of glandular involvement elsewhere in the mediastinum.

At thoracotomy, a large lobulated mass was found in the anterior mediastinum adherent to the aorta. Most of the mass was removed but a small part of the tumor could not be removed because of infiltration into the aorta. Histologic examination showed the tumor to be a lymphadenoma and although no thymic tissue could be identified the tumor was presumed to have arisen in the thymus.

Pneumomediastinography in this patient demonstrated that the mediastinal mass was adherent to the aorta, and, in retrospect, one might have concluded that the tumor was inoperable and that the patient might have been treated by radiotherapy alone.



Fig. 7. Case III. Lateral tomogram. Lymphadenoma possibly arising in thymus. The gas has outlined a mass lying in the anterior mediastinum anterior to the ascending arch of the aorta. Gas failed to dissect between the aorta and the mass and at operation the mass was adherent to the ascending arch, preventing complete removal.

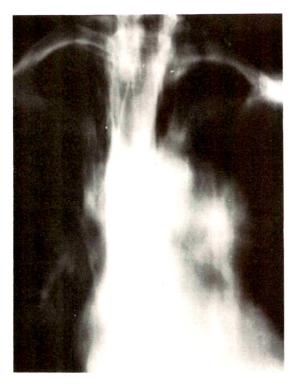


Fig. 8. Case III. Anteroposterior tomogram (same patient as in Figure 7) shows an extensive mass extending across the whole anterior mediastinum. Gas fails to pass between the mass and the surrounding structures.

PARATHYROID ADENOMA

Case IV. M.R. This 55 year old woman presented with urinary infection. On investigation, she was found to have a large stag horn calculus in the pelvis of the right kidney. The serum Ca++ was 12.2 mg. per cent, serum inorganic phosphate was 1.92 mg. per cent and the serum alkaline phosphatase was 9.5 units. Examination of the neck showed 2 nodular discrete swellings in the region of the thyroid, but a scintigram (I131) showed normal distribution of functioning thyroid tissue. A chest roentgenogram showed a rounded mass in the superior mediastinum on the right side. The mass was seen to be situated mainly behind the trachea and to the right of the esophagus. The roentgenologic diagnosis rested between an aneurysm of the innominate artery and a tumor mass lying in the anterior mediastinum. Pneumomediastinography clearly demonstrated the rounded mass in the right of the superior mediastinum and showed it to be situated lateral to the trachea and posterior to the superior vena cava and separate from the innominate artery (Fig. 9). There was no evidence of aberrant parathyroid tissue in the anterior mediastinum. Some enlargement of the right lobe of the thyroid was demonstrated.

The neck was explored and an enlarged lower parathyroid gland was found within the upper mediastinum and removed. Histologically, the parathyroid gland was adenomatous and had undergone cystic degeneration.

This case illustrates the application of pneumomediastinography to the investigation of parathyroid adenoma.

MEDIASTINAL LYMPHADENOPATHY

Case v. A.C. This 62 year old man presented with bilateral cervical and axillary lymphadenopathy of undetermined duration. Cervical lymph node biopsy established a diagnosis of lymphosarcoma. Although conventional roentgenograms of the chest showed no abnormality, mediastinal lymphadenopathy was clearly demonstrated at pneumomediastinography (Fig. 10). Ten months later he required abdominal

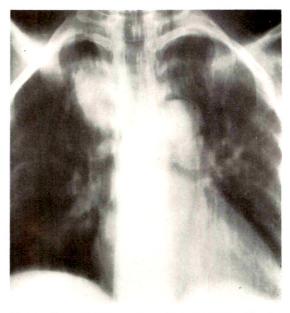


Fig. 9. Case IV. Anteroposterior tomogram. Hyperparathyroidism. Large mass in the right superior mediastinum outlined by gas. The azygos vein and aortic knuckle are also shown. In other tomographic cuts, the innominate artery could be identified medial to the mass. At operation, a parathyroid adenoma with cystic degeneration was excised.



Fig. 10. Case v. Anteroposterior tomogram of a patient with lymphosarcoma of cervical and axillary lymph nodes. Gas has outlined an enlarged lymph node in the right superior mediastinum. There are probably 2 other small lymph nodes present, 1 in each hilus.

radiation therapy following the development of a central abdominal lymphoid mass.

This case illustrates that conventional roentgenography may fail to demonstrate mediastinal lymphadenopathy. The use of pneumomediastinography may enable more accurate assessment of tumors of the reticulo-endothelial system.

CARCINOMA OF BRONCHUS

Case vi. W.C. A male patient, aged 63 years, with a carcinoma of the left main bronchus had evidence of left recurrent laryngeal and left phrenic palsy, together with a Horner's syndrome. The clinical evidence indicated an inoperable tumor and pneumomediastinography revealed a failure of dissection of the gas around the left hilus and the pulmonary artery. A linear opacity was demonstrated alongside the mediastinum at the level of the left hilus

and this was presumed to be a plaque of neoplastic tissue (Fig. 11).

Case vii. J.B. This male patient, aged 63 years, was admitted complaining of a 2 month history of hemoptysis. A chest roentgenogram demonstrated a large opacity in the anterior segment of the left upper lobe. Pneumomediastinography showed that gas had passed along the main pulmonary artery and into the aortic window. The first part of the left pulmonary artery was also outlined by gas. The ligamentum arteriosum could be identified (Fig. 12). The aortic window was free of enlarged lymph nodes and no enlarged lymph nodes were demonstrated elsewhere in the mediastinum. At operation a solid, firm neoplasm, 5 cm. in diameter, was found near the hilus, surrounding the upper lobe bronchus. The tumor had extended along the left pulmonary artery to a point I inch distal to the ligamentum arteriosum. There

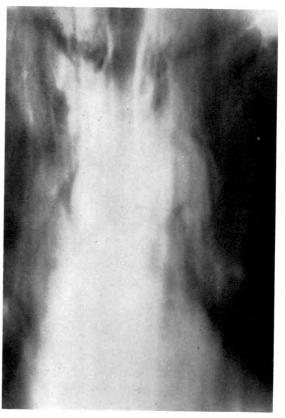


Fig. 11. Case vi. Anteroposterior tomogram. Inoperable carcinoma of the left bronchus. Gas failed to diffuse between the main pulmonary artery and the aorta and a mass is present adjacent to these structures—? plaque of neoplastic tissue.



Fig. 12. Case VII. Anteroposterior tomogram. Large malignant mass arising from the left main bronchus. Gas diffuses between the aorta and the main pulmonary artery as far as the left pulmonary artery. The ligamentum arteriosum can be identified just internal to the pleural reflection. The lung containing the tumor was removed without difficulty.

was no involvement of the mediastinum. A pneumonectomy was performed without difficulty. On histologic examination, the tumor was found to be a squamous cell carcinoma, and it had infiltrated to a point I cm. distal to the divided bronchus.

These 2 cases (Case VI and VII) illustrate the possibility of using pneumomediastinography to determine the operability of bronchial carcinoma, particularly when left hilar involvement is questioned.

DISCUSSION

Condorelli⁴ in 1936 published his paper on the retrosternal method of pneumomediastinography. This method succeeds in producing adequate filling of the anterior

mediastinum and is the technique which we have favored for the outlining of the thymus. Marchand, 17 from fluid injection studies in autopsy material, concluded that fascial sheaths enclosed the great vessels, esophagus and trachea, and that these prevent the free circulation of fluid injection into the mediastinum. In common with Hughes et al.9 we have found that the mediastinum behaves differently when gas is injected. Gas tends to diffuse widely through the mediastinum and also upwards into the neck. After injection of gas into the anterior mediastinum using the retrosternal method, gas will pass into the posterior mediastinum, particularly if the patient is turned into the prone position. However, filling of the posterior mediastinum is not so adequate compared with the transtracheal method.

Other techniques of pneumomediastinography include the injection of gas through a needle inserted directly through the manubriosternal joint into the anterior mediastinum.14 Baccaglini,1 Betoulieres et al.,3 Isard et al.,12 and Tapiovaara20 used the presacral method of insufflation, allowing the gas in the retroperitoneal space to pass upwards into the mediastinum. This method was employed because the danger of gas embolism was considered to be less than in the direct approaches. According to Hughes et al.,9 the presacral method is unreliable and in our experience a large amount of gas must be injected, producing much discomfort. Šimeček and Holub, 19 while investigating patients with suspected bronchial carcinoma, injected gas through a needle inserted through the tracheal wall during bronchoscopy. Berne et al.2 performed routine scalene lymph node biopsies in patients with suspected bronchial carcinoma, and as an extension of the procedure they injected gas through a catheter introduced into the mediastinum through the operation site. When the retrosternal technique could not be used because of masses lying in the thoracic inlet, Hughes et al.9 inserted a needle upwards into the anterior mediastinum behind the xiphisternum.

In our experience the retrosternal method gives satisfactory delineation of the thymus although the technique cannot distinguish between the relative proportions of lymphoid tissue, fat and connective tissue within the thymus. In a series of 44 patients with thyroid disease, roentgenologic enlargement of the thymus was frequently noted in those who had evidence of auto-immunity. ¹¹ The retrosternal method was used by Hare and Mackay⁷ in the investigation of 12 patients with other disorders associated with auto-immunity.

Keynes,13 in a series of 155 patients with myasthenia gravis subjected to thoracotomy, found that 11.6 per cent had tumors in the thymus. Kreel, Blendis and Piercy14 believe that it is important to recognize tumors preoperatively in order to plan the correct treatment. Pneumomediastinography will clearly outline thymic tumors as in the case reported in this paper. Harper and Guyer⁸ believe that tumors of the thymus should always be delineated by tomograms taken at suitable depths and with suitable projections. Kreel¹⁵ has been able to demonstrate small tumors by pneumomediastinography in 2 patients with severe myasthenia gravis where straight roentgenograms and tomograms revealed no abnormality. A similar case is described in the present paper. If a thymic tumor does not encroach on the mediastinal borders, it is unlikely to be visualized by conventional roentgenography.

Posen et al. 18 described a patient with primary hyperparathyroidism who had normal conventional roentgenograms, but on pneumomediastinography a mass was demonstrated in the superior mediastinum, and this proved to be a parathyroid adenoma at operation. In Case IV of the present paper, a parathyroid adenoma was clearly delineated at pneumomediastinography and at subsequent operation a parathyroid adenoma was removed. The clear demarcation of the thyroid at pneumomediastinography together with I 131 scintiscans also helps to resolve the differential diagnosis of a superior mediastinal mass

seen by conventional roentgenography. Delineation of the thyroid by gas may also be of value in providing an objective measurement of thyroid size and be helpful in performing a needle biopsy of the thyroid.

In Case v of the present paper, the chest roentgenograms were negative in a patient with lymphosarcoma involving cervical and axillary lymph nodes. At pneumomediastinography, enlarged mediastinal lymph nodes were clearly demonstrated. This finding is of some importance in determining the grading of the disease, its treatment and its prognosis. It is anticipated that lymph nodes of I cm. in diameter might be identified by this means.

While the diagnosis of carcinoma of the bronchus may be established by the use of techniques including roentgenology, bronchoscopy and possibly lung biopsy, the possibility of a successful resection is much more difficult to determine before thoracotomy. While venography and angiography may determine, to some extent, the degree of lymph node involvement and mediastinal spread, these methods are limited. Only lymph nodes that lie close to the superior vena cava will cause distortion of that structure. Bronchial arteriography will not necessarily show up all the lymph nodes involved and may not indicate the extent of the spread of the tumor. Thoracic surgeons have particular difficulty in assessing the spread of growth from a left hilus tumor towards the mediastinum. Šimeček and Holub,19 using the pertracheal method during bronchoscopy, examined 500 patients with carcinoma of the bronchus and found the method of considerable value in assessing involvement of the mediastinal lymph nodes and the extent of mediastinal infiltration. They claim to be able to exclude patients who have inoperable tumors from unnecessary thoracotomy and from the roentgenologic appearances claim that they can differentiate between enlargement of mediastinal lymph nodes due to tumor from those due to inflammation. Ikins et al.10 introduced a catheter through the operation wound following

scalene lymph node biopsy. Large amounts of carbon dioxide, from I up to 8 liters, were injected into the mediastinum. In a series of 3I patients with bronchial carcinoma, they found the method of considerable value in assessing the degree of lymph node metastases and mediastinal infiltration. We have performed insufficient examinations to assess fully the usefulness of the method but believe that pneumomediastinography has a place in the investigation of patients with carcinoma of the bronchus with a view to excluding patients with inoperable carcinoma from unnecessary thoracotomy.

SUMMARY

Pneumomediastinography is a safe procedure provided the technique is carried out with proper precautions against gas embolism. The transtracheal and retrosternal methods of Condorelli⁴ have been performed on 110 patients without morbidity.

The method has been employed for the investigation of the thymus, the parathyroid glands, mediastinal lymphadenopathy and the thyroid gland. The possibility of using the method to assess operability of bronchial carcinoma is discussed.

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MEDIASTINAL LIPOMATOSIS SECONDARY TO STEROID THERAPY*

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In A discussion of Cushing's syndrome, Keel and Neil¹ state, "The corticoids are known to mobilize and break down reserve fat, but the clinical findings suggest that in this syndrome a redistribution of reserve fat occurs, *i.e.*, mobilization followed by deposition elsewhere." The upper mediastinum is one area where this mobilized fat may be accumulated to the extent that a mass lesion is evident on chest roentgenograms. It is the purpose of the authors to call attention to this possibility in patients on prolonged steroid therapy.

In 2 of the 3 patients reported here, an exploratory thoracotomy established the diagnosis. The third patient died of other causes and the suspected diagnosis was confirmed at autopsy.

REPORT OF CASES

CASE I. E.A., a 57 year old white woman, was admitted to Hartford Hospital, Hartford, Connecticut, on January 25, 1965, for evaulation of an asymptomatic mass in the mediastinum which had been gradually increasing in size since 1962. The patient had taken 7.5 mg. prednisone daily for at least 5 years because of bronchial asthma. A chest roentgenogram in 1959 was unremarkable. In 1965 symmetric upper mediastinal widening was obvious (Fig. 1, A, B and C).

On exploration, a fatty mass was found to occupy both sides of the upper mediastinum. It extended down to the arch of the aorta and about the innominate artery and vein. A thyroid adenoma, which measured 1.5 cm. in greatest diameter, and the masses of fat were removed. The histologic diagnosis was colloid thyroid adenoma and adipose tissue.

Case II. G.B., a 35 year old white man, was admitted to Strong Memorial Hospital, Roch-

ester, New York, on April 5, 1964, with a history of bronchial asthma since the age of 5 years. The disease had become steadily more severe during the preceding 10 years and prednisone therapy was begun in June, 1962. The average dose was 20 mg. although as much as 80 mg. per day was given at times.

Gradual widening of the upper mediastinum was noted in sequential chest roentgenograms (Fig. 2, A, B and C) at the patient's place of employment and this led to the present admission. At physical examination, Cushingoid facies was noted. There were no other abnormalities.

When the patient was explored on April 10, 1964, the right superior mediastinum contained soft, scattered masses of fatty tissue. The aorta, superior vena cava and other upper mediastinal structures were thoroughly examined for other disease but none was found.

Case III. E.M., a 63 year old white man, was admitted to Strong Memorial Hospital on December 22, 1965, following the onset of signs and symptoms suggestive of a stroke. The patient had had dermatitis of uncertain etiology for 15 years during which time he had received suppressive doses of corticosteroids (75 mg./day). In the last 6 years his face had developed a moon-like appearance and he had gained weight, from 140 to 189 pounds. Several months prior to admission, he had developed symptoms compatible with subacute bacterial endocarditis.

Physical examination showed a moon-faced, obese, febrile patient with a generalized dermatitis and a diastolic murmur over the aorta. A chest roentgenogram showed symmetric widening of the upper mediastinum (Fig. 3). His course was rapidly down hill with weakness of the right upper limb and stupor developing on January 5, 1966. He died 5 days later.

At autopsy, considerable fat was found throughout the body, including the upper part of the mediastinum. Endocarditis of the aortic

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valve and multifocal encephalomalacia due to thrombi were present.

DISCUSSION

All 3 of these patients had in common a history of prolonged systemic steroid therapy. The roentgenologic findings consisted of similar symmetric widening of the upper mediastinum. This feature was sufficient to raise the suspicion of the presence of a significant mediastinal mass and led to thoracotomy in 2 of the patients.

Although the roentgen findings alone might not have permitted the making of a definite diagnosis, they did possess features that would rarely be expected with mass lesions such as lymphomas, metastatic disease, thymomas, substernal thyroid or encapsulated lipomas. The smooth symmetric widening extended from about the lung roots up to the thoracic inlet. There were no pressure effects on the trachea as would be expected with firm or encapsulated lesions.

Ancillary signs such as osteoporosis with fractures of vertebral bodies or ribs might suggest the correct diagnosis and lead to inquiry about steroid therapy. Sequential chest roentgenograms, as were available in Cases I and II, show the gradual enlargement of the mediastinum over several vears. The only other site where increase in

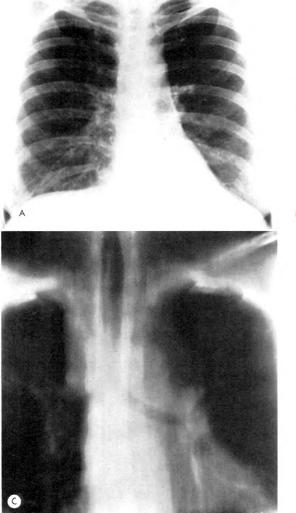
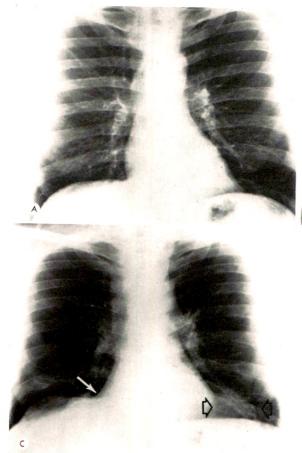




Fig. 1. Case 1. (A) 1959: Normal chest. (B) 1965: Symmetric, smoothly outlined superior mediastinal widening without tracheal narrowing. (C) 1965: Tomographic confirmation.



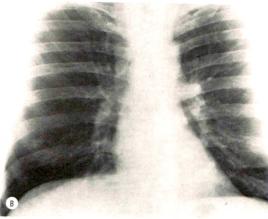


Fig. 2. Case II. (A) 1959: Normal mediastinum. (B) 1963: Bilateral superior mediastinal widening. (C) 1965: Note accumulation of epicardial fat bilaterally (arrows).

fat deposition was recognized retrospectively was the pericardial fat pad (Fig. 2C). This may prove to be another hint of the fatty nature of the mediastinal mass.

In a review of the recent literature and standard textbooks, no reference could be found to this roentgenographic finding in patients with Cushing's disease or those on prolonged steroid therapy. It is hoped that awareness of this condition will enable the radiologist to make the correct diagnosis before surgery is undertaken.

SUMMARY

Three patients with unusual amounts of fat accumulation in the upper mediastinum due to prolonged steroid therapy are reported.

A smoothly outlined, symmetric mass



Fig. 3. Case III. 1965: Bilateral superior mediastinal widening in posteroanterior upright roentgenogram.

density in the upper mediastinum without pressure effect on the trachea in an asymptomatic patient with this history should suggest the correct diagnosis.

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A ROENTGEN DIAGNOSTIC OBSERVATION IN SUBPLEURAL LIPOMA*

By RAYMOND GRAMIAK, M.D., and HERBERT J. KOERNER, M.D. ROCHESTER, NEW YORK

INTRATHORACIC lipomas are rare tumors. Those in a subpleural position without an extrathoracic component represent only a small fraction of the entire group.⁴

The diagnosis of intrathoracic lipoma is usually made by needle biopsy or surgical exploration. The fatty nature of these tumors with their attendant radiolucency and semifluid consistency has permitted the following roentgenologic observations from which a correct diagnosis can be made.

Heuer³ noted a peripheral radiolucency in a large mediastinal mass and concluded correctly that it was a lipoma. Dolley and Brewer² added the observation that mediastinal lipomas may transmit the cardiac impulse with a characteristic undulating motion. A change in shape in a large intrathoracic lipoma was recorded by Wiper and Miller⁵ when the patient was studied upright and in the Trendelenburg position. Cesanelli, as quoted by Keeley and Vana,⁴ used diagnostic pneumoperitoneum to demonstrate flattening of a lipoma lying in contact with the right diaphragm.

This report is based on 2 cases of subpleural lipoma in which another diagnostic feature was seen, namely, a change in shape of the lesion during respiration.

REPORT OF CASES

Case I. (M.C.) This 62 year old ex bartender was admitted to Rochester Municipal Hospital, Rochester, New York, on December 4, 1952, with arteriosclerotic heart disease, Laennec's cirrhosis, umbilical hernia and benign prostatic hypertrophy. Roentgenograms of the chest demonstrated cardiomegaly and a sharply demarcated mass projecting into the left hemithorax in the posterolateral aspect.

He was readmitted 9 months later because of

a fractured fibula. Roentgenologic examination of his chest showed no significant difference from the previous study. Fluoroscopy at this time added the observation that the mass appeared to be soft and was deformed by the respiratory motions (Fig. 1, A, B and C).

The patient refused all further diagnostic and therapeutic procedures. He died I year later and autopsy revealed a very soft yellow slightly pedunculated mass, measuring 7 cm. in diameter, bulging the parietal pleura outward over the left posterior rib cage. Microscopically, this was a benign lipoma.

Case II. (S.B.) This 56 year old man was admitted to Park Avenue Hospital, Rochester, New York, September I4, I961, with a history of a mass in the left hemithorax discovered on routine roentgenographic examination made at his place of employment. He gave no history of acute or chronic illness and had no complaints relative to his chest. Examination of the thoracic wall showed no abnormality. Roentgenograms of the chest demonstrated a mass showing the

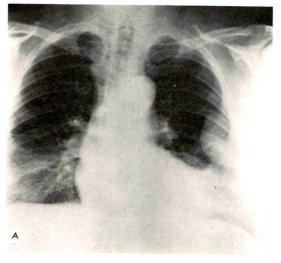


Fig. 1. (A) The posteroanterior chest roentgenogram shows an extrapleural density laterally in the midportion of the left lung field.

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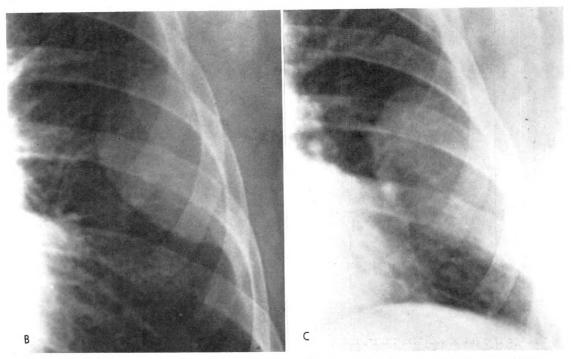


Fig. 1. (B) During inspiration, there is a marked flattening of the lesion as contrasted with its appearance during expiration (C). Note also the increased radiolucency of the mass (C).

characteristic features of an extrapleural tumor. Fluoroscopically, it appeared to change shape, becoming flatter during deep inspiration (Fig. 2, A, B and C). The ribs appeared normal and there was no evidence of cardiac or pulmonary disease. The roentgenologic conclusion was soft extrapleural tumor, probably a lipoma.

A left thoracotomy was performed 4 days following admission and a subpleural lipoma was removed. The pathologic examination revealed an encapsulated piece of adipose tissue which measured 7 by 7 by 1.4 cm. and proved at microscopic examination to be a benign lipoma. The patient was discharged on the fourteenth hospital day in good condition.

DISCUSSION

The diagnosis of intrathoracic lipoma should be considered in any smoothly marginated, extrapleural tumor which is unassociated with rib abnormalities and which can be compressed by the expanding lung. Berne and Heitzman¹ reported 2 cases of pleural mesothelioma with changes in shape attributed to rotation of the mass on a pedicle during respiration. Their lesions differed from ours in that they were attached to the visceral pleura and, therefore,

moved relative to the thoracic cage.

Loculated fluid due to congestive heart failure, trauma, or an inflammatory process



Fig. 2. (A) An extrapleural density is seen in the left lower lung field.

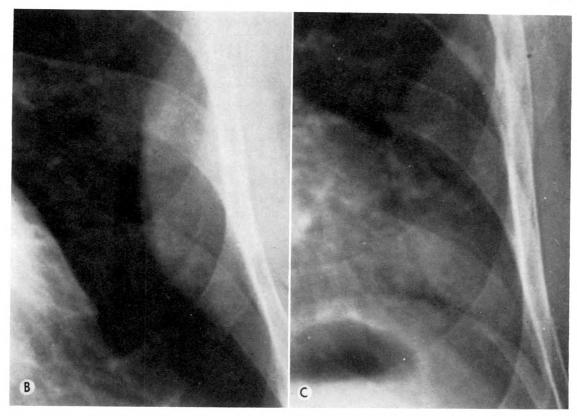


Fig. 2. Comparison of the spot roentgenograms made at inspiration (B) and expiration (C) reveals an over-all diminution in the size of the mass during inspiration with some local flattening of the contour inferiorly. Also, a band-like density which projects over the base of the lesion disappears during expiration. This line is probably pleural in origin and related to compression of the lipoma.

can mimic the findings as seen in patients with subpleural lipomas. A separation of these entities should be possible with history, other secondary supporting signs, and serial examination.

Primary or metastatic disease to a rib shows local osseous change and a hard consistency which precludes an alteration in shape with respiration.

SUMMARY

Two cases of subpleural lipoma are reported in which a characteristic flattening of the contour with deep inspiration could be demonstrated fluoroscopically and in spot roentgenograms. It is suggested that this finding is typical of subpleural lipomas.

Raymond Gramiak, M.D. Division of Diagnostic Radiology Strong Memorial Hospital Rochester, New York 14620 Appreciation is expressed to Dr. Theophil Artemowych for permission to use the clinical records of the second case and to Dr. Robert S. Weiner for his report of the surgical findings. We are indebted to Mr. William S. Cornwell, Clinical Associate in Radiology, for his valuable editorial assistance.

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CLINICAL AND PATHOLOGICAL REACTIONS TO THE BRONCHOGRAPHIC AGENT DIONOSIL AQUEOUS*

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A CLINICAL and pathological study of the use of dionosil aqueous* was undertaken to determine the efficacy of this material as a bronchographic agent at the University of Maryland Hospital. A concomitant toxicity study using rabbits was also done.

In the clinical study, 175 bronchographies were done from January, 1964 to September, 1965, and these patients were followed for at least 2 months after bronchography. Thirteen of these patients had subsequent pulmonary surgery at varying intervals after bronchography and the resected specimens were histologically examined to determine if any pathologic changes were incurred by bronchography.

ANIMAL STUDIES

Forty rabbits weighing approximately 2 kg. each were divided into 3 groups. Anesthesia was accomplished with 50 mg. of nembutal/kg. intravenously. Utilizing aseptic technique, the trachea was exposed below the cricoid cartilage. The first group (16 rabbits) received an intratracheal injection of 0.3 cc. of dionosil aqueous /kg. of body weight which corresponds to the amount usually required for bilateral bronchography in humans. The second group (16 rabbits) received 0.9 cc. of dionosil aqueous/kg. of body weight; a third group (8 rabbits), which also underwent anesthesia and operation but received no intratracheal material, served as

controls. Chest roentgenograms were taken to determine the distribution of contrast material, and adequate bilateral bronchograms were apparent. Four animals from the 0.9 cc. and 0.3 cc./kg. group and 2 each from the control group were sacrificed 2, 7, and 21 and 60 days following bronchography. All the viscera were examined grossly. The lungs were fixed in 10 per cent formalin and paraffin sections were stained with hematoxylin and eosin.

Microscopic examination with polarized light of unstained smears of carboxymethylcellulose and dionosil aqueous revealed birefringent particles which were more intense and more colorful in the latter. Smears of dionosil aqueous were subjected to routine staining with hematoxylin and eosin and this material appeared as unstained irregular particles and "spaces" with a light amphophilic outline varying from several to 40 microns. Birefringence was not present in the stained smears of dionosil aqueous; this quality apparently is lost in the staining process.

Gross examination of the lungs of the 0.3 and 0.9 cc./kg. group sacrificed at 2 days post bronchography and 0.9 cc./kg. animals sacrificed at 7 days revealed scattered, somewhat ill-defined tan-white foci throughout the parenchyma. No gross abnormalities were apparent in any of the remaining animals.

In animals sacrificed at 2 days, histologic examination of the lungs revealed scattered collections of inflammatory cells, predominantly macrophages with some polymorphonuclear cells, lining or filling large and smaller bronchi and bronchioles (Fig.

^{*} Dionosil Aqueous (n-propyl ester of 3:5-diodo-4-pyridone-N-acetic acid, suspended in water, with sodium carboxymethyl-cellulose, sodium citrate, sodium chloride, polyethylene glycol 600 mono-oleate and benzyl alcohol).

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FIG. 1. Photomicrograph of the lung of a rabbit receiving 0.9 cc./kg. of dionosil aqueous and sacrificed in 2 days. A large bronchiole is filled with inflammatory cells, predominantly polymorphonuclear. Unstained particulate matter is scattered about (H & E, ×250).

1). Distributed among the inflammatory cells were irregular particulate appearing spaces similar to those seen on the stained smear of the contrast medium and some scattered amorphous eosinophilic material. The cytoplasm of many of the macrophages was abundant, eosinophilic, and granular. Small irregular unstained or slightly eosinophilic particles were present in some. Focal collections of granular macrophages and polymorphonuclear leukocytes in bronchial walls and peribronchial areas were present. Scattered foci of pneumonitis with irregular unstained particulate spaces and cells similar to those present in the bronchial tree were present in the parenchyma. Only an occasional giant cell was present in this and the 7 day 0.9 cc./kg.

group. Varying degrees of congestion of the alveolar walls and patchy areas of pink, proteinaceous fluid in the alveolar spaces were present. Changes in both the 0.3 and 0.9 cc./kg. groups were similar but more pronounced in the latter.

The lungs of animals receiving 0.9 cc./kg. and sacrificed in 7 days (Fig. 2) showed scattered small bronchi and bronchioles filled with collections of macrophages with abundant eosinophilic cytoplasm. Irregular particulate-like spaces similar to those already described were scattered about. Focal collections of granular macrophages were present in some of the bronchial walls and peribronchial areas. No polymorpho-

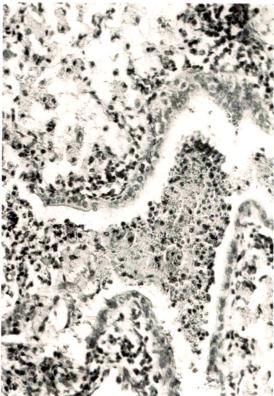


Fig. 2. Photomicrograph of the lung of a rabbit receiving 0.9 cc./kg. of dionosil aqueous and sacrificed in 7 days. A bronchiole present in the center is filled by numerous granular macrophages. Particulate matter is present, predominantly within macrophages but some is extracellular, scattered among eosinophilic debris. Similar macrophages are present in alveoli adjacent to the bronchiole (H & E, ×250).

nuclear cells were present. In the parenchyma of I animal, there appeared to be several areas of early organization with granular macrophages, some erythrocytes and a few fibroblasts and capillary buds. In several small bronchi in this animal, there were intraluminal collections of macrophages with some fibroblasts covered by bronchial epithelium (Fig. 3). Some of these were contiguous with the bronchial walls. Again, irregular unstained particulate-like spaces were present and

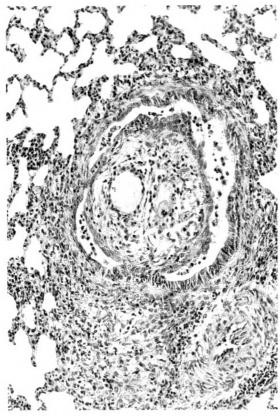


Fig. 3. Photomicrograph of the lung of another rabbit receiving 0.9 cc./kg. of dionosil aqueous and sacrificed in 7 days. In the lumen of a large bronchiole is a nodular-like collection of mononuclear cells and some fibroblasts, partially covered by bronchial epithelium. Within this nodule are particulate-like spaces which do not stain. Surrounding the bronchiole and in some of the adjacent alveolar spaces is an infiltrate of mononuclear cells and granular macrophages similar to those in the preceding photomicrographs. These changes were not present in the 3 week or 2 month groups (H & E, ×165).

scattered macrophages appeared to contain some smaller unstained fragments.

In the animals receiving 0.3 cc./kg. and sacrificed at 7 days, the bronchial system appeared clear. A few focal collections of granular macrophages were present in the alveoli.

In the 3 week animals, which received 0.9 cc./kg., occasional foci of macrophages, some of which appeared quite granular, were present in the parenchyma and bronchioles. Particulate spaces were not definitely identifiable, but occasionally were quite suggestive. There was no evidence of organization. Thus, changes seen in the earlier animals appeared to be completely resolved. In the 0.3 cc./kg. animals, only a few macrophages were scattered about the alveolar spaces.

In the 0.9 cc./kg. 2 month animals, a few eosinophilic granular macrophages were present in the parenchyma. The lungs otherwise appeared normal. In the 0.3 cc./kg. animals, no abnormalities were apparent.

Fat, iron and connective tissue stains on each group were not significant. Although P.A.S. positive material was present in some of the macrophages, this could not definitely be correlated with the bronchographic agent. Also there was no specific correlation apparent with toluidine blue stains. No birefringence was present in any of the animals. Control animals from each group were unremarkable except for peribronchial collections of lymphocytes.

HUMAN STUDIES

In the clinical group, dionosil aqueous was used as the contrast agent in 175 consecutive bronchographies. Adult patients received 100 mg. of nembutal and 0.4 mg. of atropine intramuscularly approximately 1 hour prior to the procedure, and local anesthesia was accomplished by spraying the pharynx and larynx with 2 per cent xylocaine. Studies in children were done under general anesthesia, utilizing a special endotracheal tube with a side hole adapter to accommodate the catheter. No unto-

ward reactions from the premedication or the local anesthesia were encountered. A rubber catheter was inserted transnasally through the larynx into the trachea, and anesthesia of the bronchial mucosa was accomplished by injecting 2 cc. of xylocaine into each lung. The bronchi were outlined with dionosil aqueous under fluoroscopic control, and appropriate roentgenograms were made. Twenty to thirty cc. of contrast material was generally required for adequate bilateral bronchograms.

The patients in this group ranged in age from 14 months to 78 years. There were 133 males and 42 females. The most common clinical indications for bronchography were chronic cough, hemoptysis, unresolved pneumonia or an abnormal chest roentgenogram. Seventy-five bronchograms (43 per cent) were normal. Bilateral studies were done in 54 cases (31 per cent).

The most common pathologic diagnoses were bronchiectasis and chronic bronchitis. Alveolarization of contrast material was not a problem, being present to a slight degree in 12 per cent of patients. No postbronchographic complications were found in 105 patients (60 per cent), while 34 patients had minimal temperature elevations of 99 to 100°F. for 1 to 2 days. Eighteen patients (10 per cent) had temperature spikes to 101°F. for 1 to 2 days, and another 18 patients (10 per cent) had temperature elevations to 102°F. for 1 to 2 days. None of the patients in this study developed clinically apparent "postbronchographic pneumonia.'

Thirteen of the 175 patients had pulmonary surgery (lobectomy or pneumonectomy) at various intervals after bronchography, and areas remote to the primary disease focus were studied histologically. The intervals between bronchography and surgery ranged from 5 days to 4 months. In 2 patients, 7 and 8 day post bronchography, surgical specimens revealed foci in the pulmonary parenchyma consisting of numerous granular macrophages and irregular particulate-like spaces similar to areas present in the experimental animals. No

other inflammatory cells or other possible etiologic agents were apparent. In the remainder of the surgical specimens, no pathologic changes could be detected in the bronchial systems or pulmonary parenchyma attributable to bronchography.

DISCUSSION

The object of our present study was to investigate the efficacy of dionosil aqueous as a bronchographic agent and to determine if there were any adverse reactions to this material. Previously, we had reported on some clinical and experimental observations with hytrast* bronchography, utilizing the same procedure as reported for the present study. This agent appeared as birefringent particles in the lungs of rabbits and humans and evoked an early polymorphonuclear reaction followed by an intense mononuclear response with foreign body giant cells (Fig. 4). Phagocytosis of the particles was a prominent feature, and some of the bronchographic material appeared in the peribronchial lymphatics. Morphologically, residuals of this agent with cellular reactions were present in tissue sections from rabbit and human post hytrast bronchographic pulmonary tissue for considerable periods (37 days in human lung and 2 months in rabbit lung). Thus, this series of reactions and persistence of contrast material vary somewhat from those under present study in that dionosil aqueous is not birefringent in tissue sections and resolution appears virtually complete in 3 weeks.

Clinically, it was found that both dionosil aqueous and hytrast are adequate media for outlining the bronchial tree. Hytrast does give slightly more contrast but this is due to its higher iodine content. Subjectively, hytrast appears to be somewhat more irritating to the bronchial mucosa than dionosil aqueous in that patients tend to cough more during the examination

^{*} Hytrast (3,5-Diiodopyridone-430.5% w/v, N-(2,3-propyl-diol)-3,5-Diiodopyridone-446.0% w/v, sodium carboxymethyl-cellulose, methyl and propyl parabens, monosodium phosphate and water).

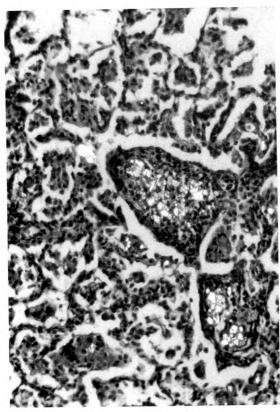


Fig. 4. Photomicrograph of a section of rabbit lung 3 weeks after hytrast bronchography. In an alveolar duct and adjacent alveoli are varying sized birefringent particles which are surrounded and/or phagocytized by many of the numerous macrophages present (H & E, partially crossed polaroids, ×250).

when the former is used as the bronchographic agent. Moderate postbronchographic pyrexia was noted in 20 per cent of patients with both hytrast and with dionosil aqueous; however, in 175 consecutive cases using dionosil aqueous no postbronchographic pneumonias occurred while with hytrast 2 severe cases of pneumonia were encountered in 75 examinations.

It is believed that the ability to obtain equally good bronchograms with either hytrast or dionosil aqueous is related to their common suspending agent, carboxymethylcellulose, in that this material renders these media viscous, allowing them to cling to the bronchial mucosa sufficiently long to secure roentgenograms and to prevent excessive alveolar filling.

The dionosil aqueous that remains in the lungs after bronchography appears to follow 2 main avenues of elimination. The radiopaque portion (propyliodone) is most likely hydrolized, absorbed and excreted via the kidneys. To support this concept are the reported I131 tracer studies that reveal iodine in the urine soon after bronchography begins; and, in addition, the majority of the instilled iodine can be recovered from the urine within 72 hours.6 Also, it has been reported5 that radiopaque material can be visualized in the kidneys on survey roentgenograms of the abdomen after bronchography with umbradil.* Apparently, the suspending portion of dionosil aqueous follows a different avenue of elimination. The phagocytic cellular response following dionosil aqueous bronchography in the experimental animals and in the human surgical specimens would suggest that macrophages are important in the elimination of the suspending material from the pulmonary system. Once phagocytized, the carboxymethylcellulose could either be eliminated by expectoration or the particles reduced in size and eliminated by way of the lymphatics. The response is similar to that described by Hellström and Holmgren² using carboxymethylcellulose instillation alone into the lungs of rats and rabbits. We did not observe foreign body granuloma in either the experimental animal or the human lung as reported by Hess³ after instillation of carboxymethylcellulose into 19 human lungs.

Any of the commonly used bronchographic media will induce a cellular reaction. This reaction varies with the technique employed, amount of contrast material used, and the composition of the agent, *i.e.*, radiopaque portion and suspending vehicle. Although dionosil aqueous also evokes a cellular response, this material appears to be promptly eliminated from the lungs and no residual histologic damage is apparent in experimental animal or human pulmonary tissue. Resolution of any pulmonary

^{*} Umbradil: diethamolamine salt of 3,5-diiodo-4-pyridone-Nacetic acid suspended in carboxymethylcellulose. (A.B. Astra.)

changes appears virtually complete 3 weeks after bronchography with dionosil aqueous; while following hytrast bronchography, contrast material and an associated cellular reaction existed in the lungs for as long as 3 months.

SUMMARY

Clinical and experimental observations with dionosil aqueous and hytrast bronchography reveal a pulmonary inflammatory reaction to both media. Much of this reaction appears to be related to their common suspending agent, carboxymethylcellulose, but differences exist which are probably related to the radiopaque portions of the media. Adequate bronchograms can be obtained with either material, but the clinical reaction appears to be less frequent and less severe with dionosil aqueous.

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BRONCHIAL BRUSHING IN THE DIAGNOSIS OF PERIPHERAL LUNG LESIONS*

A PRELIMINARY REPORT

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THE determination of the etiology of solitary spherical lesions and nonspecific infiltrations in the periphery of the lung beyond the reach of the bronchoscopist is a constantly recurring clinical problem. In the majority of lesions of this type, the histologic diagnosis is not established prior to thoracotomy. 16 The importance of establishing a diagnosis in these cases becomes even more critical when one realizes that the majority of primary lung neoplasms arise not in the major bronchi accessible to the bronchoscopist but in the segmental and subsegmental divisions of the lobar bronchi.8 Brewer and his colleagues1 have also pointed out that the highest rate of resectability of lung cancers and the highest survival rate is in those tumors situated in the midzone of the lung which are not accessible to the bronchoscopist. While published series reveal a considerable variation in the incidence of malignancy in so-called coin lesions, 10,18 there is some agreement that many, if not the majority, of the lesions arising in patients over 45 years of age are malignant. It should also be realized that while a nonspecific parenchymal lesion in a younger person is less likely to be malignant, in Davis and co-workers's series, 20 per cent of the lesions occurring in patients under 45 vears of age were malignant. In many of these cases, a thorough clinical investigation, including examination of the sputum for tubercle bacilli and abnormal cells will reveal the etiology of the lesion. All too frequently, however, the true nature of the nonspecific infiltration or mass seen on the chest roentgenogram remains obscure.

In an attempt to provide a better specimen for the cytologist and bacteriologist,

we have developed a technique which frequently clarifies the diagnosis in otherwise obscure lesions. Essentially, this technique consists in introducing a radiopaque preshaped catheter under fluoroscopic control into the segmental or subsegmental bronchus in which the lesion is situated. Standard gray arterial catheters of the type described by Ödman¹⁵ are used. These are preshapeable, radiopaque and disposable. After the catheter has been positioned, small brushes are passed through it and advanced toward the lesion and, if possible, into its substance. Microscopic slides are prepared directly from the brushes; following this, the area is irrigated with Ringer's solution and the washings are retained for bacteriologic examination.

TECHNIQUE

The patient takes nothing by mouth for 4 to 6 hours prior to the examination and receives pre-medication with seconal and codeine ½ hour before coming to the Department of Radiology. The dose of premedication is varied to suit the patient's age and general condition. The catheter is preshaped prior to the examination, the exact shape depending upon the portion of the bronchial tree to be catheterized.5 For example, to enter the apical segment, a curve of at least 180 degrees is necessary. A somewhat similar configuration but with the addition of a short curve projecting anteriorly or posteriorly near the tip of the catheter is used for the other upper lobe segments. A 90 degree curvature is ideal for the middle lobe and ventral or dorsal segments of the lower lobe and lesser degrees of curvature for the remaining lower lobe segments. Shaping of the catheter is facil-

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itated by having a previous bronchogram for guidance but in most cases this is not necessary. Topical anesthesia of the upper airway and one nostril is obtained by spraying with a topical anesthetic solution as for bronchography. The larynx is anesthetized by the introduction of 2 to 3 cc. of topical anesthetic through a curved metal cannula inserted over the tongue. After satisfactory topical anesthesia has been obtained, the preshaped catheter is lubricated with a viscous anesthetic, a No. 205 guide wire is inserted in it, stiff end first to straighten the curvature, and the catheter and guide wire are inserted in the anesthetized nostril. When the tip of the catheter touches the posterior wall of the nasopharynx, the guide wire is withdrawn slightly, permitting the catheter to curve into the oropharynx. The guide wire is then withdrawn entirely and reinserted with the flexible end protruding 2 to 3 cm. beyond the tip of the catheter to form a relatively soft leading point. In our first series of patients the catheter was advanced through the larynx with the stiff end of the guide wire about I cm. proximal to the tip of the catheter. Recently we have abandoned that practice because of the potential danger of damaging the vocal cords. The catheter and guide wire are observed fluoroscopically and positioned over the vocal cords. During deep inspiration producing abduction of the cords, the catheter and guide wire are gently passed into the trachea and the tip positioned just above the carina. At this stage, the guide wire is again removed and 3 to 5 cc. of topical anesthetic is injected. The guide wire is again repositioned with the flexible end protruding slightly from the catheter and the catheter is advanced in the main bronchus on the side of the lesion. After entering the main bronchus, it is often advisable to inject an additional 3 to 4 cc. of anesthetic; however, care must be taken to limit the total amount of anesthetic used because of the possibility of a reaction to the anesthetic agent.

After the catheter has been positioned in the main bronchus, its curvature may be

varied as desired by advancing or retracting the guide wire, and, by judicious manipulation under fluoroscopic control, it is usually a simple matter to place the tip of the catheter in the desired segmental orifice. Once this has been achieved, the catheter is advanced distally and placed as close as possible to the lesion. Roentgenograms are obtained for confirmation of the position. Occasionally, at this stage in the procedure it is determined that the catheter is not correctly shaped to enter the desired segment; if this is the case, it is a simple matter to remove the catheter over the guide wire, alter the curvature as desired, and then reinsert it again over the guide wire.

After a satisfactory position of the catheter has been achieved, small cylindrical nylon brushes (Fig. 1, a, b and c) are passed through it toward the lesion and, if possible, into the lesion. By making slight changes in the curve of the tip of the brush, it is possible to vary the direction of its passage through the bronchial tree. Several brushes are used and specimens are obtained from peripheral bronchi in and around the lesion. Microscopic slides are prepared at once from the brushes and are fixed immediately in 95 per cent alcohol. Following this, the region is irrigated with Ringer's solution and the washings are retained. The slides and washings are subsequently examined for bacteria and abnormal cells. The brush itself may be used to inoculate a culture medium after it has been introduced into an abscess or other inflammatory lesion. After the specimens have been obtained, selective or routine bronchography may be performed using the same catheter.

Facility with the technique is readily acquired; the method is simple and in our experience has been free from complications of any type. Figures 2 through 8 show patients in whom the technique has been used.

DISCUSSION

It has been pointed out by Brewer and his colleagues¹ that the largest number of resectable lung cancers lie in the midzone

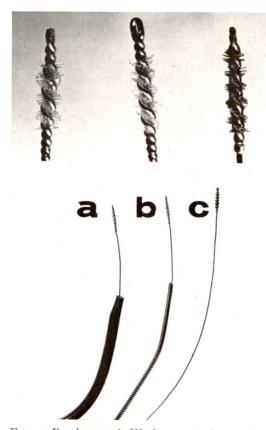


Fig. 1. Brushes used. We have experimented with various types of brushes; however, those illustrated above have proved the most useful so far. (a) and (b) have bristles of 0.005 Tynex nylon wound in a helix of 0.014 stainless steel wire. The wire is 36 inches long. It is continuous with the helix of the brush to eliminate the possibility of losing the brush in the periphery of the lung. The over-all length of the rigid portion of the wire, in other words the helix, is 6.5 mm. and the over-all length of the bristle containing portion is 3.9 mm. The total diameter of the bristles is 1.3 mm. Brush (c) is identical to (a) and (b) except that the bristles consist of 0.002 stainless steel. This latter brush sometimes provides a better specimen but it is more difficult to prepare a slide from this

(a) illustrates the brush protruding from the tip of the catheter. (b) illustrates a brush inserted through the outer portion of a guide wire from which the core has been removed. It is sometimes necessary to insert the brush in this manner when the catheter is sharply curved, as, for example, when it is positioned in the apical segment of the upper lobe since the upper leader of the brush is not firm enough to enable one to exert sufficient pressure to force the brush around the sharp curvature of the catheter. (c) illustrates the brush removed from the guide wire.

of the lung and are inaccessible to the bronchoscopist. Examination of the sputum will reveal abnormal cells in a majority of these cases as has been demonstrated by Frenzel and Papageorgiou.⁶ However,

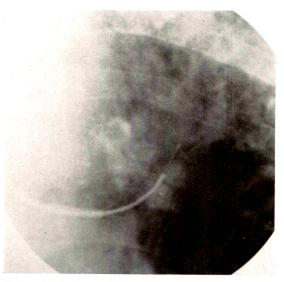


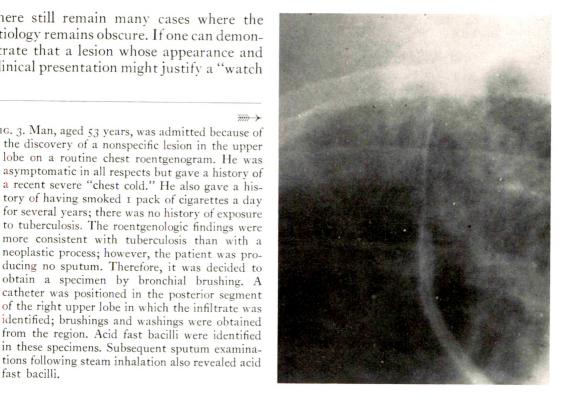
Fig. 2. Man, aged 68 years, presented with chronic cough, hoarseness of 6 weeks' duration, approximately 20 pounds weight loss over 4 weeks and dyspnea on exertion for 2 weeks. On examination, he appeared thin, pale and lethargic with diminished breath sounds over the left upper lobe and hepatomegaly. He was moderately anemic. Chest roentgenograms showed a diffuse infiltration involving the upper lobe on the left with several areas within the infiltration suggesting cavitation. Roentgenologically, it was not possible to determine if the findings represented an active granulomatous infection or small abscess cavities distal to a bronchogenic carcinoma. Bronchoscopy revealed no specific abnormalities and a biopsy specimen obtained at bronchoscopy revealed one clump of atypical cells which were not diagnostic of carcinoma. The patient was not able to produce sufficient sputum for diagnostic purposes even with the aid of steam inhalation. The left upper lobe bronchus was selectively catheterized; an obstruction was encountered at the bifurcation into the apical and posterior segments. Brushings and washings were obtained from this region and revealed cells consistent with a poorly differentiated carcinoma. Following the brushing, selective bronchography was performed confirming an obstruction of the segmental bronchus. The illustration demonstrates a brush in position; in this case the brush was inserted with the aid of the outer sheath of a guide wire as demonstrated in Figure

fast bacilli.

there still remain many cases where the etiology remains obscure. If one can demonstrate that a lesion whose appearance and clinical presentation might justify a "watch

Fig. 3. Man, aged 53 years, was admitted because of the discovery of a nonspecific lesion in the upper lobe on a routine chest roentgenogram. He was asymptomatic in all respects but gave a history of a recent severe "chest cold." He also gave a history of having smoked I pack of cigarettes a day

for several years; there was no history of exposure to tuberculosis. The roentgenologic findings were more consistent with tuberculosis than with a neoplastic process; however, the patient was producing no sputum. Therefore, it was decided to obtain a specimen by bronchial brushing. A catheter was positioned in the posterior segment of the right upper lobe in which the infiltrate was identified; brushings and washings were obtained from the region. Acid fast bacilli were identified in these specimens. Subsequent sputum examina-



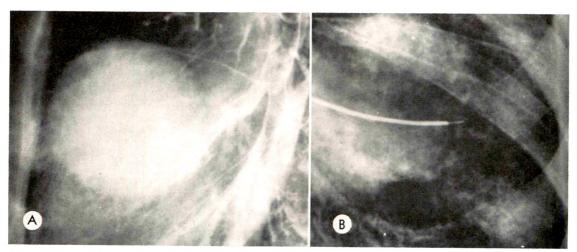


Fig. 4. Man, aged 65 years, presented with a history of shortness of breath for 6 months, moderate dyspnea on exertion, tiredness, lassitude, and occasional blood-tinged sputum. He had a chronic cough for many years, had smoked I pack of cigarettes per day for many years and had been treated for pulmonary tuberculosis 4 years previously. He had noted no loss of weight. On examination he appeared thin, but was in no acute distress. Coarse rales were noted over the right base, and there was a Grade II apical systolic murmur. Physical examination was otherwise essentially negative. Chest roentgenogram revealed a round, well circumscribed mass in the middle lobe on the right (A). This mass had no specific internal characteristics and had well defined margins. At bronchoscopy, it was noted that the orifice of the middle lobe appeared somewhat narrow but had smooth margins. A biopsy obtained at bronchoscopy revealed bronchial mucosa with focal squamous metaplasia. Bronchial brushing (B) revealed abundant highly atypical cells consistent with malignancy. This patient subsequently underwent radiation therapy followed by pneumonectomy.





Fig. 5. Man, aged 73 years, had a 30 pound weight loss in 3 months. He had been followed in the out-

and wait" policy is in fact malignant, one renders a very significant service to the patient. The contrary also holds true in that demonstration of tuberculosis or other benign process in an apparently malignant lesion would prevent an unnecessary thoracotomy. A further application of this method is the recovery of organisms from parenchymal lesions in patients unable to produce sufficient sputum for diagnostic purposes, even with the aid of steam or saline inhalation.

From time to time various methods have been proposed to overcome the difficulties in making the diagnosis in cases of non-specific lung lesions. MacLean¹¹ has used a similar approach to ours, passing a brush through a bronchoscope into the orifice of the segmental bronchus containing the lesion. He has described cylindrical nylon brushes with detachable and disposable tips. The diameter of the brush head is approximately 5 mm., which limits its use to the larger segmental bronchi.

Fridel⁷ has described a technique for

patient department for several years because of obstructive lung disease and hypertension with congestive heart failure. He had also noted increased tiredness, lassitude and a recent onset of hoarseness. Prior to the onset of symptoms, he had smoked I pack of cigarettes per week for several years. On examination, he appeared thin but in no acute distress. However, labored respiration appeared on mild exertion. There were decreased breath sounds in the left base posteriorly. At bronchoscopy, no mass was seen but there was some narrowing of the main bronchus; a biopsy obtained at bronchoscopy revealed squamous metaplasia and chronic bronchitis. Subsequently, bronchial brushing was performed (A); the specimen revealed cells exhibiting highly atypical features strongly suggestive of malignancy. Bronchography performed at the same time (B) revealed rather marked narrowing of the lower lobe bronchus and distention of bronchial glands in the lingula consistent with bronchitis. Because of the obstructive lung disease, no therapy was undertaken in this patient. The patient's subsequent course confirmed carcinoma with development of a pleural effusion and deterioration in the general condition.

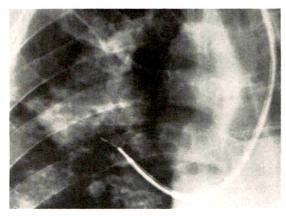


Fig. 6. Man, aged 57 years, had left pleuritic pain for 10 days. He had also noted a chronic, nonproductive cough, mild dyspnea on exertion, anorexia and a 10 pound weight loss over several weeks. He gave a history of having worked in a brick factory sawing bricks for 9 years and had smoked a pack of cigarettes a day for several years. On examination, he appeared well developed and in no acute distress. The chest roentgenogram revealed findings consistent with silicosis with masses in both upper lobes. There was no definite roentgen evidence of active tuberculosis or neoplasm. Repeated sputum examination and bronchial washings at bronchoscopy revealed no abnormalities. Bronchial brushing was performed and specimens were obtained from the region of both apical masses. While neither tubercle bacilli nor tumor cells were recovered, there was abundant doubly refractile material consistent with silica to confirm the diagnosis of silicosis. Because of the strong possibility of tuberculosis occurring in the silicotic masses, the patient has been treated with antituberculous chemotherapy with improvement in his symptoms.

passing a radiopaque catheter peripherally through the bronchial tree under fluoroscopic control and obtaining a specimen for examination by irrigating the region. The catheter is introduced through a bronchoscope as in MacLain's technique and its passage is monitored by the fluoroscopist. The addition of fluoroscopy is an improvement over the MacLain method; however, it is difficult and dangerous to move the patient with a bronchoscope in position and localization of an instrument within the bronchial tree in a frontal projection alone is not always possible.

Nordenström and Carlens¹² have used a small alligator-type biopsy forceps in-

serted through a preshaped bronchography catheter. This instrument is small enough to reach into the segmental bronchi but is too large to pass peripherally. It appears an ideal instrument for obtaining specimens from tumors obstructing segmental bronchi. The specimen obtained is sufficiently large not to be ruined by the presence of contrast material in the bronchial tree and this enables the radiologist to obtain a biopsy specimen immediately if the bronchogram reveals an intraluminal mass.

Hattori *et al.*⁹ have added a further refinement in an effort to obtain specimens from peripheral lesions. They have described two types of brushes to be introduced through a Metras catheter. One is a

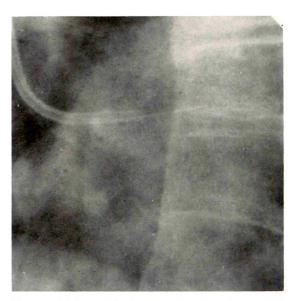
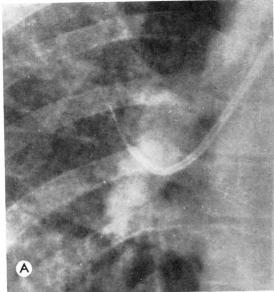


Fig. 7. Male, aged 60 years, had weakness and marked weight loss. On examination, coarse rales were noted overlying the left lower lobe posteriorly. The patient also had signs of hyperthyroidism and mild congestive failure. Chest roentgenograms revealed a mass suggestive of a neoplasm involving the superior segment of the left lower lobe. Bronchial brushing recovered cells consistent with carcinoma. Two subsequent sputum examinations revealed no abnormal cells. A third sputum examination revealed markedly atypical cells, but they were too few in number for diagnostic purposes. A bronchogram made following bronchial brushing demonstrated a stenosis of the superior segmental bronchus.



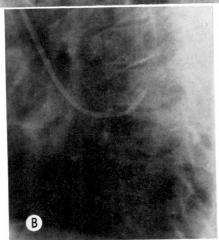


Fig. 8. Man, aged 52 years, was admitted from the emergency room with a history of chills and fever for I week. There was no history of alcoholism or of unconsciousness. The admission chest roentgenogram revealed an abscess cavity in the superior segment of the right lower lobe. On physical examination, the patient appeared somewhat emaciated but otherwise normal. At bronchoscopy purulent material was seen coming from the orifice of the superior segmental bronchus of the right lower lobe. The lesion was initially treated with penicillin; however, this had to be discontinued because of an allergic reaction. Following this, the segmental bronchus was selectively catheterized; brushings (A and B) and washings were obtained from the abscess. These revealed no growth of organisms presumably because of exposure to penicillin. Following the brushing, I gm. of chloromycetin was instilled into the cavity.

simple spiral brush with a flexible handle and in general principle is similar to ours. The other has an elbow-like hinge near the tip, enabling the operator to vary its direction with ease. They report a high rate of accuracy in recovering diagnostic material from very small lesions in the periphery of the lung. Dr. Hattori has been kind enough to provide us with samples of the brush and we have found them extremely useful. The only possible disadvantage noted in their use is the necessity to clean and resterilize the brushes after each use, and, of course, the potential, though unlikely, hazard of losing the flexible tip in the lung periphery. It is our impression that a disposable instrument such as we have described has a certain advantage in that it is used only once and then discarded together with the catheter through which it was introduced. This removes all possibility of cross-infection or of spurious positive cytology specimens.

Needle biopsy or aspiration biopsy of pulmonary lesions would appear to be a simple and effective method of providing a histologic diagnosis in many cases and descriptions of techniques for performing this examination have been published.^{2,17} This method has not been very extensively employed in the United States because of the potential hazard of tumor spread along the needle tract and chest surgeons have advised against its use,^{4,14} at least, in potentially operable lesions. This method has been extensively employed in Sweden, however, by Nordenström.¹³

The cavity subsequently closed and the patient has done well since that time. Certainly, one cannot claim from this that the introduction of antibiotic directly into the lesion was responsible for the excellent response since this might well have resulted from systemic chloromycetin which was also administered. However, it seems reasonable to assume that in certain situations this therapeutic approach would be worthwhile.

SUMMARY

A technique for obtaining material for cytologic and bacteriologic examination from the midzone and periphery of the bronchial tree is described. Essentially this technique consists of selective catheterization of the appropriate segmental bronchus with a radiopaque arterial catheter and then passing small brushes* through the catheter into the region of the lesion. Brushings and washings are obtained for cytologic and bacteriologic examination. The method is simple and in our experience has been entirely free from complications.

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INTRATHORACIC VOLEMIC EVENTS BY TETRAPOLAR ELECTRICAL IMPEDANCE DETECTION

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FUNCTIONAL indices of blood volume pulsation and volume ventilations of each lung are attainable without trauma or anesthesia in man. Detection of the modulations of an imposed radiofrequency signal to the chest leads to such volemic information. Tetrapolar impedance plethysmography as described by Nyboer,⁵ Allison et al.,^{1,4} and Bonjer² is applicable to such methodology. The results by impedance plethysmography compare favorably with similar studies through the chest made by independent x-ray densigraphy by Marchal, Marchal and Kourilsky³ and also by direct bronchospirometry.

METHODS AND RESULTS

A dual tetrapolar electrical impedance plethysmograph is arranged to record impedances transversely on the posterior and/ or anterior chest (Fig. 1). This is a constant current device and similar to a Kelvin double bridge. The electrodes, usually made of aluminum foil, are supported on plastic and pressed firmly against the skin with or without conductive paste. The capacitative impedance is nulled, the base resistive impedance is noted and the changes in resistive impedance recorded and calibrated. The amplifier gain of each unit is reproducibly adaptable to sensing pulmonary vascular pulses, cardiac pulsation, and tidal, forced and held respirations (Fig. 1).

Pulses are best recorded during suspended respiration. The parameters of displacement or displacement per second are sensed as ohms or ohms per second. This is equivalent to the series resistive effect of parallel resistive event. Our present units have a direct output of I volt or 0.I volt per 0.I ohm difference. These voltage signals are transferable to equations in computer amplifier systems for translation to units of volume and/or volume per second, or percentile signals representing $\Delta R/R$. Pulsatile volume or ventilation per minute within each zone is calculated from direct or extrapolated measures by multiplying the appropriate excursion by its repetitive rate or factor.

Two units of electrical impedance plethysmography, slaved to each other at 100 kilocycle frequency, are used in chest spirometry. The current electrodes are held in each mid-axilla. The resistance between the spine and right post-axillary electrodes also normally contains variations, ΔR ,

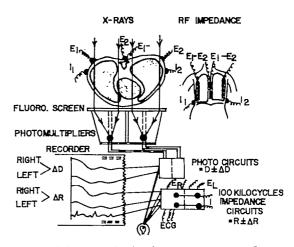


Fig. 1. Schema of simultaneous roentgenfluorodensigraphy and tetrapolar electrical impedance spirometry of right and left chest. I₁ and I₂ represent current electrodes for radio frequency signals; E₁ and E₂ independent voltage detection electrodes for each hemithorax; R±ΔR=resistance±change in resistance; D±ΔD=roentgen density±change in density.

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related to respiration and pulse volume in the established electrical field. Similar conditions are present on the left posterior chest. Each chest segment of 15 cm. measures about 10 ohms. The variations due to forced breathing fluctuate about 2 ohms, to tidal breathing 0.2 ohm and to vascular pulsation about .02 ohm. The fluoroscopic screen shows variations in luminescence with variations in respiration and vascular pulsation. This is empirically detected by photomultipliers for each chest zone, calibrated and recorded simultaneously with electrocardiographic and impedance events.

The result of a simultaneous study by x-ray and radiofrequency impedance spirograms is shown while the subject is standing (Fig. 2). Tracings are made of events in the right and left lungs during forced respiration. A tabular summary of measurement is listed below this study.

Functional differences in impedance associated with tidal respiration reveal a superimposed regular irregularity due to intrathoracic and chest wall vascular pulsations. Inspiration is associated with an increase in electrical resistance (Fig. 3, *left*). If respiration is suspended voluntarily,

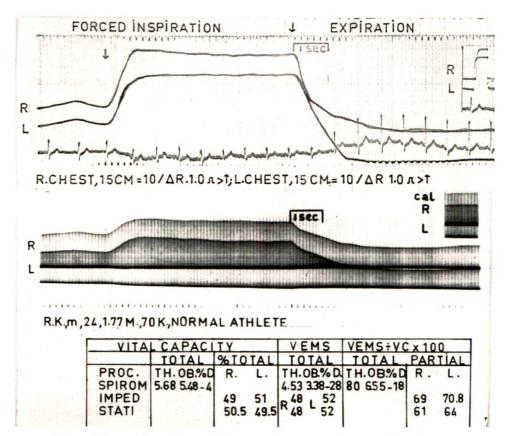


Fig. 2. Bilateral impedance spirograms and x-ray densigrams. Abbreviations:

R = right	VEMS ÷ VC × 100 = Tiffeneau ratio
L = left	Proc. = procedure
$\Delta R = \text{ohms resistance } (R)$	Spirom = mechanical spirogram
M = meter	Imped = impedance spirogram
K = kilogram	Stati = x-ray densigram
m = male	TH = theoretical
VC = vital capacity	OB = observed
VEMS=maximum expired volume per second	D = +/- percentile deviation
CM = centimeter	cal = calibration

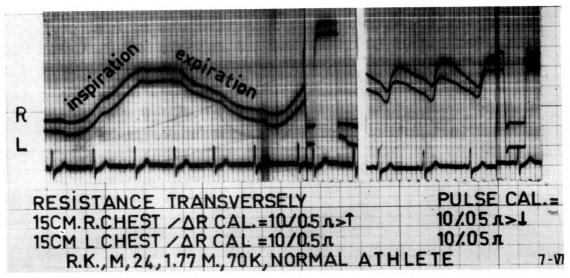


Fig. 3. Left: Electrical impedance spirogram during tidal breathing of same normal subject as in Figure 2. Right: Vascular pulsation of right and left chest and lungs during suspended breathing simultaneously with electrocardiogram. Standards of ΔR as indicated.

amplifier gain increased and the polarity of the output reversed, simultaneous volume pulsations are recorded correctly from each hemithorax. The increase in volume is recorded up. A decreased electrical resistance with systole occurs in the posterior lung zones of a normal subject (Fig. 3, right). This poses a physical question as to whether this pulsation is primarily derived from the lung or the chest wall. Studies



Fig. 4. Anteroposterior roentgenogram of a patient, postoperatively, after a complete pneumonectomy for severe bronchiectasis.

over the anterior chest are not always similar to the posterior chest observations. The following cases assist us in comprehending the basic changes.

Measurement of a case of right pneumonectomy 4 months after the operation shows a lower segmental electrical resistance on the right than on the left. Respiratory activity during forced ventilation and tidal breathing is minimal on the right side (Fig. 4 and 5). Each is measurable. The abnormal right effects are produced by the shifting mediastinal mass, the change in its chest content and possibly some lung transfer from the intact side. The right chest is much less pulsatile than the left as the pulsatile lung has been removed. The residual vascular pulsation detectable by our methods is probably due to vessels in the chest wall only.

In a normal subject, symmetric detection of 10 cm. of anterior chest to the right of the mid-sternum also shows an increased electrical conductance with lung pulse systole (Fig. 6). On the other hand, 10 cm. to the left over the precordium shows a decreased conductance electrically with systolic emptying of the heart. A series electrical resistive addition of these 2 segments

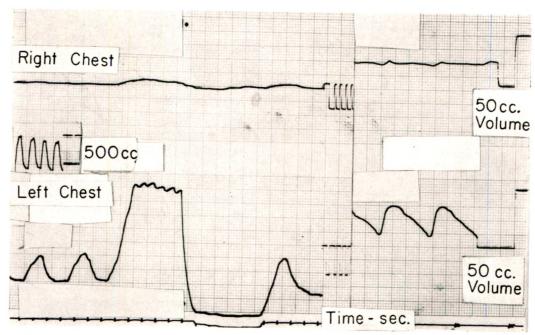


Fig. 5. Same case as in Figure 4. Bilateral impedance spirograms 4 months after pneumonectomy for severe bronchiectasis. The right chest measured 7.0 ohms and the left chest measured 9.5 ohms per 15 cm. transversely, and the total of 30 cm. measured 17.5 ohms. The small residual pulse on the right is derived from the chest wall. (Subject male, 22 years of age, 65 kilograms, 1.72 meters.)

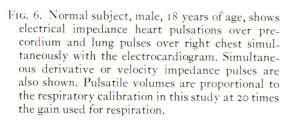
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(20 cm.) yields a nondescript volume pulsation involving cancellation due to phase differences in the heart and lung pulsations. If, however, a 30 cm. segment is studied anteriorly on this subject, the positive pulmonary vascular pulse dominates the field in spite of the inclusive cardiac pool. These results resemble pulse information

from the posterior chest of normal subjects (Fig. 7).

COMMENT AND CONCLUSIONS

Electrical impedance measurements have a great deal of bearing on blood distributions during respiration and the cardiac cycle. These are related to ionic elec-

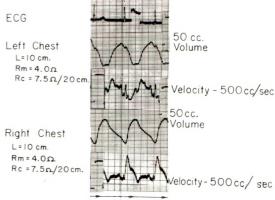




L=length

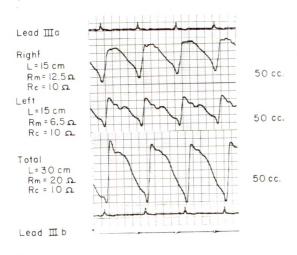
R_m=measured resistance

 $R_e =$ computer resistance when 1 liter inspiration has equal excursion to an impedance of 1 volt output from the unit



Time - sec.

TRANSVERSE ANTERIOR CHEST (Recumbent)



Time - sec

Fig. 7. Similar study to that in Figure 6; however, distance between detection electrodes is increased to 15 cm. for the right and left chest and 30 cm. for the total. Note that the precordial volume pulse in Figure 6 is not present in the left chest study as the lung pulses dominate the larger segment.

trical conduction and parallel electrical resistive shunts. This type of study deserves correlation with displacement, velocity, acceleration and force types of ballistocardiography and spirometry. Electrical impedance is a convenient tool for study of the central as well as the peripheral circulation. Quantitative percentile relations existing between right and left chest pulmonary functions are helpful in assessing effects of pulmonary disease, pulmonary surgery, pulmonary therapy and pulmonary rehabilitation progress from a dynamic viewpoint. The authors and others are engaged in evaluating the precordial volume pulse with stroke volume. Instrumentation for resistive impedance measurement is best understood for volemic deter-

minations from Kelvin double bridge measurements. The impedance method has no contraindications for patient examination as it is nontraumatic, nonstimulating and isothermal in its characteristics on the body segments, including the eye.

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THE APPLICATION OF THE IMPEDANCE PNEUMOGRAPH TO CHEST ROENTGENOGRAPHY

A USEFUL MEDICAL BY-PRODUCT OF THE SPACE PROGRAM

By E. NICHOLAS SARGENT, M.D.,* THOMAS L. ROBERTSON,† EARL V. WAGONER, Jr.,‡ and BERNARD J. O'LOUGHLIN, M.D.§ ORANGE, CALIFORNIA

RADITIONALLY, respiration has been recorded by the use of pneumographs, pneumotachographs, spirometers, strain gauges, negative pressure transducers, 5,9,10 and crystal thermistor sensors. 12 Difficulties encountered with pneumographs include leaks in the air systems and slippage on the body, along with problems of locating a level where the maximum chest or abdominal expansion occurs. Pneumotachographs and spirometers are excellent quantitative instruments which indicate air velocity and volume, but these, and crystal thermistor sensors, all require connection to airways by means of face masks, mouth or nose pieces. Recording intratracheal or intrapleural pressures with negative pressure transducers is only practical in laboratory animals or with anes-

That the human body possesses electrical resistance and capacitative properties has been well documented. 2,11 Resistance variations, associated with respiration, are more pronounced than capacitance changes. Impedance spirometry is practical because of functional relationships between transthoracic impedance and the volume of respired air in the lungs. With calibration of the impedance pneumograph, there is demonstrable a linear relationship between transthoracic impedance and tidal volume.4-8 The transducer is merely a pair of electrodes and, because of this, it even becomes possible to obtain an electrocardiogram from the same pair of electrodes, if desired. However, the electrical resistive

impedance method does not directly measure the air entering and leaving the lungs in biologic segments. The resulting changes in conductivity associated with pulmonary volume variations are considered to be manifestations of redistribution of blood volume and variations in tissue resistivities, with the electrical properties of the body acting as a three dimensional conductor. There is, from an electrophysical viewpoint, a sleeving effect by the expanding dielectric containing lungs, for electrical current pathways.1,8

The impedance method for recording respiration offers many practical advantages. Existing volume determining devices, such as conventional spirometers, pneumotachometers and crystal thermistor sensors, because they require direct contact with the air stream in operation, create loading on the air stream and are directly contaminated by the patient. Thermistor crystal sensors activate the x-ray machine near peak inspiration and are not usable at peak expiration. Strain guage and torso belt sensors are inconvenient, tend to slip and may show troublesone artifacts on the exposed film. The impedance pneumograph results in only limited, indirect contamination of the detection electrodes by the patient, eliminates many of the above objections, and yet, maintains a high degree of accuracy. It is a stable transducer for respiration, easy to apply to individuals of all sizes and ages, and reflects the volume of air exchange readily with minimal restraint or discomfort to the subject.

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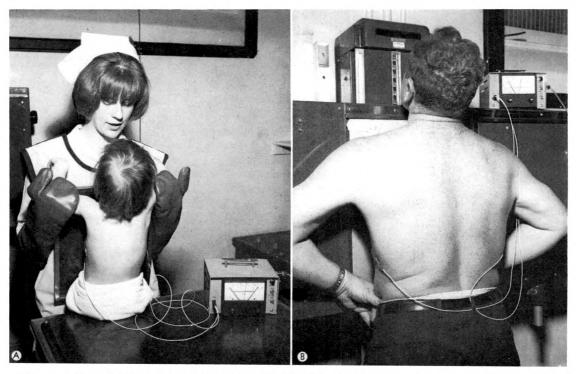


Fig. 1. (A) Application of electrodes to chest of child. (B) Application of electrodes to chest of adult.

An automatic x-ray exposure device for chest roentgenography has long been desirable. By applying the principles of impedance pneumography to suitable circuitry, an automatic triggering device at any desired phase of respiration is possible. The fundamental principle of the impedance pneumograph, as applied to chest roent-

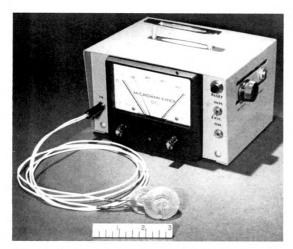


Fig. 2. Impedance pneumograph showing large deflection scale on meter with attached electrodes.

genography, is the measure of a small change in impedance with respiration (about 5 per cent) across the thoracic cage. Two electrodes (Ag–AgCl), applied with conductive electrocardiographic jelly are taped on the skin of the chest and are the only contact with the patient (Fig. 1, A and B).

The basic equipment required for measurements by the impedance change method is a high frequency oscillator which sends a current through the electrodes placed appropriately on the body and suitable circuitry to measure the small current changes accompanying respiration. The greatest impedance change is found to be located in the midaxillary line at approximately the level of the sixth rib.⁵

Instrument design considerations incorporated are simplicity of operation for nontechnical personnel, technician and patient acceptance, a large display meter, remote display capabilities (meter, scope, recorder) and battery operation for portability and safety. The electronics section of the instrument includes an impedance

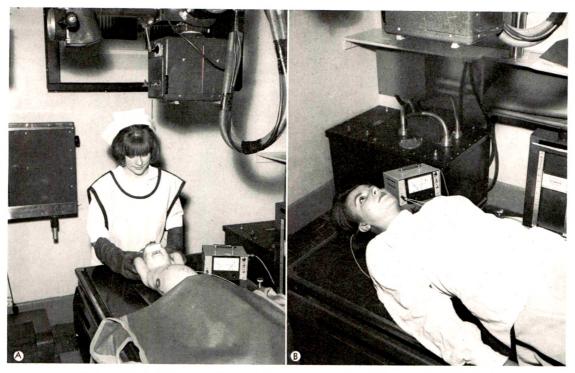


Fig. 3. (A) Child in recumbent position with attached electrodes. (B) Adult in recumbent position with attached electrodes.

pneumograph, a meter relay and controller with external control and adjustments (Fig. 2). The size of the instrument is determined by the size of the display meter, since the electronics package requires less space than the battery required for operation. There is no mechanical inertia in the system and the subject can be studied erect, sitting, prone recumbent, supine, laterally and during and after exercise (Fig. 3, \mathcal{A} and \mathcal{B}).

A three position switch permits the operator to activate the x-ray exposure manually or automatically on maximum inspiration or maximum expiration (Fig. 4, A–D). The signal is utilized by connecting to the exposure circuit of the x-ray machine. The triggering is automatic while the rotor of the rotating anode of the x-ray tube is operating, with the time of exposure at any pre-selected level of respiration as determined by the operator. A sensitivity switch is incorporated so that the meter sensitivity can be adjusted for infants and adults.

The unit has been in practical operation,

and is acceptable to the x-ray technician and to the patient. It is extremely accurate in making the roentgenographic exposures at any desired time. The machine is especially useful in obtaining roentgenograms with maximum inspiration or maximum expiration in children and in noncooperative adults. It is light in weight and portable and can be easily applied to fixed or portable installations. It is clean, noncontaminating, easily applied to the patient and easily sterilizable. It is relatively low in cost, and decreases the number of "retake" examinations, thus decreasing the added radiation exposures to the patient and surrounding personnel. When used in association with an automatic cassette changer, two roentgenograms can automatically be made in inspiration and expiration.

As a future research device, it has many exciting possibilities. Future studies will include correlation of roentgenographic findings with impedance spirometry measurements, both in health and disease.

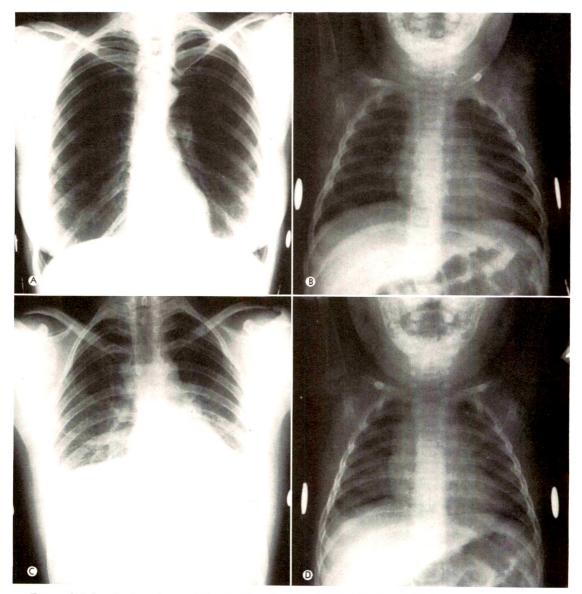


Fig. 4. (A) Inspiration chest roentgenogram of adult. (B) Inspiration chest roentgenogram of child. (C) Expiration chest roentgenogram of adult. (D) Expiration chest roentgenogram of child.

Further investigation of the correlation between impedance changes, roentgenographic chest findings and therapeutic response during the treatment of chest diseases will also be conducted.

SUMMARY

A practical application of impedance changes in the chest during respiration has resulted in an insturment which can control the time of x-ray exposure during chest roentgenography at any desired period of respiration. The instrument,* designed by North American Aviation Space and Information Systems Division, is a by-product of the Space program, contributing a useful medical device as applied to chest roent-genography.

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^{*} Patent Pending-North American Aviation, Inc.

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A COMBINATION ADULT-PEDIATRIC CHEST UNIT

By DONALD B. DARLING, M.D.* BOSTON, MASSACHUSETTS

STANDARD 6 foot erect roentgenograms of the chest are difficult to obtain without exposure of parents or hospital vices designed for infants entirely. A more feasible method would be to shield an upright cassette holder in such a fashion that personnel without the use of special de-

a child or infant could be held erect for the

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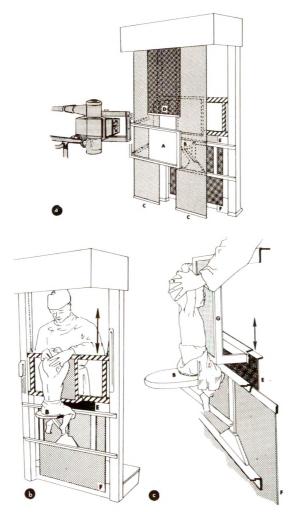


Fig. 1. Shielded chest unit showing (a) all protective shields in place, (b) the side and center lead-rubber shields removed, demonstrating a small infant held by a technician behind the rear protective shields, and (c) an insert showing how protection is maintained by the shield (E) which moves with the cassette holder.

A=Adjustable gonad shield; B=collapsible seat; C=stationary lead-rubber curtains for side protection; D=central lead-rubber curtain adjustable vertically; E=lead-rubber shield attached to bottom of cassette holder to shield space between holder and shield F; F=lead-rubber shield attached to seat support bar and extending to floor; G=cassette holder with plexiglass front and leaded back.

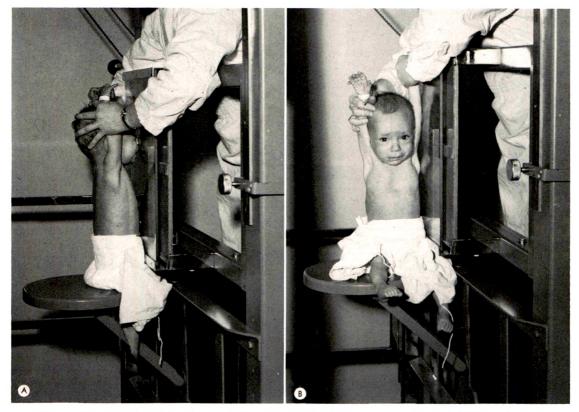


Fig. 2. Photographs of the chest unit in use to obtain (A) posteroanterior and (B) lateral chest roentgenogram of an infant. Note how easily the technician can hold the patient in position.

roentgenographic study by an attendant without risk of radiation exposure.

DESCRIPTION OF DEVICE AND ROENTGENOGRAPHIC METHOD

Figure 1, a, b and c illustrates the chest device which was constructed to meet these specifications, utilizing the type of shielding introduced by Dr. John Caffey for chest roentgenography in babies. The vertically adjustable front lead-rubber curtain (D)

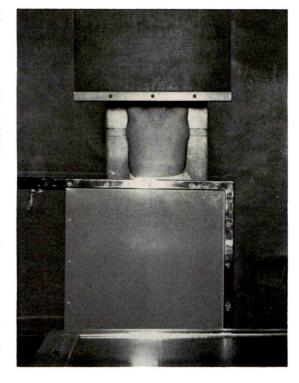


Fig. 3. Appearance of the infant for a posteroanterior chest roentgenogram as seen from the position of the roentgenographic tube. The shielding has confined all exposure to the area of the chest.

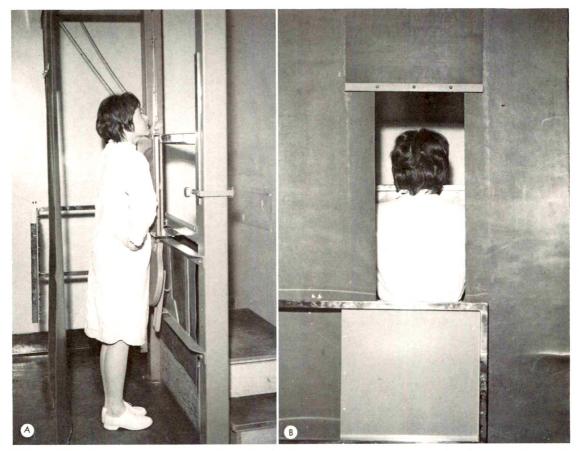


Fig. 4. Illustration of the chest unit in use to obtain a posteroanterior chest roentgenogram of an adult. (A) The seat is dropped into a vertical position. (B) Complete protection of the abdomen and pelvis by the gonad shield.

with the lead-backed cassette holder (G) and the back lead-rubber curtains (E and F) give complete protection to any person holding the patient. The stationary side lead-rubber curtains (C) shield the sides and also permit assistants to help with extremely difficult patients. In addition, an adjustable collimator with full-field illumination is used on the roentgenographic tube, although the protection of the chest device is adequate for diagnostic machines not so equipped.

Figure 2, \mathcal{A} and \mathcal{B} shows how a posteroanterior and lateral chest roentgenogram is obtained of a small infant. Note the screw type lock in Figure 2 \mathcal{A} which locks the cassette holder in position. It is important to lift the infant slightly off the seat when making the exposure. This gives the advantage of the dangling method¹ on the level of the diaphragm without the necessity to diaper-wrap the head. (Maximal inspiration can be obtained in infants by suspending them in the erect position.) Figure 3 demonstrates how the side curtains, central curtain and gonad shield effectively confine the area of exposure to the chest and completely shield the person holding the infant. We have found that the field illuminated collimator ensures that the central curtain and gonad shield are properly placed as they cast an upper and lower shadow on the patient.

Figure 4, A and B illustrates the use of the unit for chest roentgenography in adults. The collapsible seat is in the lowered

position. The gonad shield is large enough to cover the entire abdomen of an average adult and can be adjusted vertically for patients of different heights. In addition to chest roentgenography, the unit is used for erect abdominal roentgenograms in infants and small children and for erect studies of the skull in encephalography of infants.

SUMMARY

A chest unit is described that permits infants and small children to be held in the erect position without exposure to person-

nel. Details of design and illustrations of use in infants and adults are presented.

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We are indebted to Mr. Karl Burton and Picker X-Ray Corporation for the construction of the shielded chest device.

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THE AMERICAN JOURNAL OF ROENTGENOLOGY RADIUM THERAPY AND NUCLEAR MEDICINE

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Forty-ninth Annual Meeting: Royal York Hotel, Toronto, Ontario, Canada, May 29–31, 1967.

M E D I T O R I A L M

ELECTRICAL IMPEDANCE SPIROMETRY

THE variation of body electrical resistive impedance associated with measured respiratory volume was first used in 1940 by Nyboer, Bagno, Barnett, and Halsey1,2 as a calibration index of volume pulsation within the torso. The impedance method of using the ionic electrical resistance of tissues as a transducer of pulsatile mechanical functions is not widely accepted. Glasser⁸ in 1944 published our first graphic illustration of pulsatile electrical volume including that of electrical impedance changes associated with inspiration and expiration. The presence of superimposed plethysmograms of body pulsations spirited a prolonged search for a mathematical expression defining ionic electrical volume based on parallel electrical impedances and length of a given biologic conductor.

Since the fixed distance between the electrodes on the body and the specific resistivity of blood are constants, it is true then that the added volume change is inversely proportional to the variation in resistance and can be calculated quantitatively as such. The derived formula for such a quantitative determination is:

$$V_B = \rho_B \cdot l^2/R_B$$

where V_B is the volume change of blood, ρ_B the specific resistivity of blood, l the distance between electrodes, and R_B the variation in parallel resistance or impedance. In practice such determinations are of value mainly in comparison to opposite segments (e.g., right and left lungs) true normal values not being yet established for any particular body segment.

We were much encouraged in the impedance study of aeromedical physiology by the late Professor John Fulton at Yale University during the war. We recorded impedance by direct writing systems then being perfected for electrocardiography by Rahm, Dunn and myself.4 At Yale University, respiration of rats and monkeys was recorded by Gelfan and Nims⁵ during explosive decompression studies by using tetrapolar electrical impedance plethysmographic methods in simulated barometric chambers. Shortly before this time, it was shown by Bloom and his co-workers6 how positive pressure breathing reduced the amplitude of torso and peripheral volume pulsations markedly and also swelled the extremities. This last effect is indexed by a simultaneous decrease in segmental resistive electrical impedance which is caused by an over-all increase in blood storage in

Respiratory impedance waves derived from the fingers, arms, head and torso were often so large that apneic procedures were required to study the pulse unless one recorded a first derivative or velocity type of resistive impedance pulse. Respiratory effects were never considered a volume artifact by us, but a measurable function of blood redistribution. In 1955, experiments at Wright-Patterson Air Force Base⁷ indicated that we were able to define the amount of blood added to the lung caused

7 HENRY, J. P. Personal communication, 1955. Wright-Patterson Air Force Base.

¹ Nyboer, J., Baono, S., Barnett, A., and Halsey, R. H. Radiocardiograms—electrical impedance changes of heart in relation to electrocardiograms and heart sounds. J. Clin Invest., 1940, 10, 772.

<sup>19, 773.

&</sup>lt;sup>1</sup> Nувоев, J. Electrical Impedance Plethysmography. Charles C Thomas, Publisher, Springfield, Ill., 1959, pp. 243.

³ Nyboer, J. Electrical impedance plethysmography. In: Medical Physics. Volume I. Editor, O. Glasser. Year Book Publishers, Inc., Chicago, 1944.

⁴ Nyboer, J. Electrocardiogram in practical risk appraisal: introduction of direct writing electrocardiograph. The American Life Convention, Hot Springs, Virginia, 1946, June, pp. 87-98.

Life Convention, Hot Springs, Virginia, 1946, June, pp. 87–98.

**Gelfan, S., Nims, L. F., and Livingston, R. B. Explosive decompression at high altitude. Yale Aeromedical Research Report No. 66, July 1, 1047.

port No. 56, July 1, 1947.

⁶ Bloom, W. L., Kaufman, S. S., Nims, L. F., and Nyboer, J. Effect of positive pressure breathing at sea level on peripheral blood flow and cardiac output. CAM Report No. 246, 1944.

by passive elevation of the legs, or effected by counter-pressure in clothing about the lower limbs. The volume data so obtained on shifting locations of blood of human subjects with pressurized suits was comparable to that deduced by Fenn and his associates⁸ using teeter board and mechanical plethysmographic techniques. Apparently, pressurized breathing can displace about 500 cc. of blood from the lungs. This is approximately one-half the blood volume of the lungs. Much of this displaced blood is stored in the lower extremities.

Since 1959, other concerted efforts have been made to understand respiratory displacement of the chest in terms of electrical resistive impedance by Goldensohn and Zablow,9 by Allison10 for his doctorate thesis in our laboratory and by Geddes and co-workers11 in allied aerospace problems. It was also established by Nyboer12 and Nyboer, Marchal, Marchal and Kourilsky¹³ that bilateral electrical impedance spirometry and bilateral roentgen fluorodensigraphy were excellent measures of normal and abnormal degrees of functional differences within each lung. This approach is emphasized further by Nyboer, Marchal and Marchal14 in this issue of the JOURNAL, using the principle of the Kelvin double bridge with its separate current input and voltage detection electrodes. This tetrapolar method markedly decreases skin contact resistance and reduces the error of measuring a biologic conductor. Also, in this

⁸ Fenn, W. O., Otis, A. B., Rahn, H., Chadwick, L. E., and Hegnauer, A. H. Displacement of blood from lungs by pressure breathing. *Am. J. Physiol.*, 1947, 151, p. 259, Fig. 1.

⁹ GOLDENSOHN, E. S., and ZABLOW, L. Electrical impedance spirometer. J. Appl. Physiol., 1959, 14, 463-464.

10 Allison, R. D., Holmes, E. L., and Nyboer, J. Volumetric dynamics of respiration as measured by electrical impedance plethysmography. J. Appl. Physiol., 1964, 19, 166–173.

¹¹ Geddes, L. A., Hoff, H. E., Hickman, D. M., and Moore, A. G. Impedance pneumograph. *Aerospace Med.*, 1962, 33, 28–33. ¹² Nyboer, J. Bilateral pulmonary function by electrical impedance spirometry. *Harper Hosp. Bull.*, 1964, 22, 232–245. ¹³ Nyboer, J., Marchal, M., Marchal, M. T., and Kouril-

¹³ Nyboer, J., Marchal, M., Marchal, M. T., and Kourilsky, R. Pulsatility and pulmonary function of hemithoracic segments as measured by electrical impedance plethysmography and roentgendensitometry. Presented at the V. Congres International D'Angiologie, Paris, France, September 5, 1964.

¹⁴ NYBOER, J., MARCHAL, M., and MARCHAL, M. T. Intrathoracic volemic events by tetrapolar electrical impedance detection. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1966, 98, 482–486.

issue of the Journal, Sargent, Robertson, Wagner and O'Loughlin¹⁵ describe a bipolar electrical impedance technique to detect respiration and to trigger a roentgen exposure of the chest at a reproducible phase of inspiration or expiration in infants or adults. Such procedures are timely and oriented to reduce the need for technical re-exposures for making improved diagnostic roentgenograms of the chest and heart. The technique is not difficult in its application and could also be based on tetrapolar measurements of tissue impedance.

The merits of electrical resistive impedance spirometry are dependent on the simplicity and accuracy of detecting a radio signal as modulated by movements and redistribution of blood conductive content in the pulmonary arteries, capillaries and veins. If a lung is totally collapsed or removed, there is no mechanism for exchanging the ionic blood volume with breathing except to a lesser degree in the chest wall over this region. If the lung is surrounded by pleural effusion, the degree of pulmonary exchange is impaired; however, it is still detectable and measurable by impedance, although roentgenographic opaque conditions may exist. If other constrictive or obstructive factors unfavorably affect pulsatile and pulmonary exchange, impedance methods can define the percentile volumetric deviation for each lung.

Impedance spirometry can be calibrated volumetrically by breathing into a known collapsible space or through a spirometric gauge. Thereafter, the extent of function in each lung may be followed for short, protracted or repetitive study. A fairly linear relation exists between change in lung volumes and change in impedance above the resting expiratory volume. The velocity of air exchange is simultaneously recorded as the first derivative of the respiratory exchange. We may improve our ease of monitoring cardiac and pulmonary dynamics by

¹⁵ Sargent, E. N., Robertson, T. L., Wagoner, E. V., Jr., and O'Loughlin, B. J. Application of impedance pneumograph to chest roentgenography. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1966, 98, 487-491.

harnessing miniature transistor impedance units and telemeter the analogue signals while working or exercising.

Indications for such impedance study for the above conditions are to evaluate functional effects of medical and surgical therapy as well as laborious rehabilitation procedures in hospital, clinic or office. In general, we will find that electrical impedance spirometry is a collateral dynamic scientific asset to roentgen management and study of impaired lung function in asthma, pneumonia, pulmonary embolus, lung injury, postoperative pulmonary resections, cardiac bypass procedures and cardiac failure.

Percentile indices of pulmonary and other pulsatile blood flow are measurable quite directly in the imposed radiofrequency field by impedance. The early systolic runoff slope of arteriovenous volume pulses is also closely allied to the flow rate in experimental models, where flows are verified by direct collections. ¹⁶ In practice,

¹⁶ Allison, R. D., and Nyboer, J. Electrical impedance plethysmograph determination of pulse volume and flow in ionic circulatory systems. *New Istanbul Contribution to Clinical Science*, 1965, 7, 281–306.

the segmental volume pulses are corrected for venous runoff volume during early pulse systole against infinite hindrance to outflow. The product of the delivered pulse volume and the pulse rate is a practical index of pulsatile volume per minute. In the chest when these pulse exchanges are calibrated against known air-volume exchange, they bear cubic values in the order of known right ventricular and left ventricular stroke volumes. These dynamic relations, however, will require further study and scientific scrutiny with the aid of special computer circuitry.

In general, on the basis of resistive impedance or conduction of tissue, the electrical characteristics are excellent indicators of local or general volume. These are inherently useful to the functional study and diagnosis of the circulatory or respiratory status of the subject during or independent of roentgen procedures.

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NEWS ITEMS

PRE-CONGRESS INTERNATIONAL SYMPOSIUM ON THERAPY OF CANCER

On the Day Preceding the Ninth International Cancer Congress in Tokyo, Japan

An international symposium on the clinical aspects of cancer diagnosis and treatment covering various organs, sponsored by the Japanese Association for Cancer Research, Japan Society for Cancer Therapy, Japanese Medical Association, and Japanese Cancer Society, and supported by the Asahi Press and Takeda Chemical Industry, will be held at the Asahi Press Hall, Yurakucho, Tokyo, from 9:30 A.M. to 4:30 P.M. on October 22, 1966.

The speakers are Drs. T. Antoine (Austria), E. Caceres (Perú), M. Copeland (U.S.A.), M. Dargent (France), E. Easson (England), F. Gentil (Brazil), K. Hashimoto (Japan), K. Kajitani (Japan), K. Kimura (Japan), G. Pack (U.S.A.), M. Riveros (Paraguay), H. Sato (Japan), H. Shirakebe (Japan), and Y. Umegaki (Japan).

Drs. George T. Pack, Pack Medical Foundation, U.S.A., and Toru Niyaji, Osaka University Medical School, Kitaku, Osaka, Japan, will be Chairmen.

Although no charge will be made, early registration by mail is required because of the limited number of seats available.

HEALTH PHYSICS SOCIETY

FIRST MIDYEAR TOPICAL SYMPOSIUM

The Midwest Chapter of the Health Physics Society and the parent organization are sponsoring jointly a symposium on Personnel Radiation Dosimetry, which will be held January 30, 31, and February 1, 1967, at the Pick Congress Hotel in Chicago, Illinois.

The program will comprise: Legal aspects for personnel dosimetry—including round table discussion; capabilities and

adequacy of existing dosimeters and dose systems—including round table discussion; record keeping needs and requirements, value and use—including round table discussion; and new developments in personnel dosimetry.

For further information contact Jesse A. Pagliaro, Chairman, Publicity Committee, U. S. Atomic Energy Commission, Chicago Operations Office, 9800 South Cass Avenue, Argonne, Illinois 60439.

HAWAIIAN RADIOLOGICAL CONFERENCE

The Hawaiian Radiological Conference, sponsored by the American College of Radiology and the Radiological Society of Hawaii, will be held February 6, 7 and 8, 1967, at the Long House-Hilton Hawaiian Village, Honolulu, Hawaii.

The faculty comprises the following distinguished radiologists who will present courses: J. Scott Dunbar, M.D., Montreal, Quebec, Canada; Benjamin Felson, M.D., Cincinnati, Ohio; Gilbert H. Fletcher, M. D., Houston, Texas; Harold G. Jacobson, M.D., New York, New York; Manuel Viamonte, Jr., M.D., Miami, Florida; Richard H. Marshak, M.D., New York, New York; Juan M. Taveras, M.D., St. Louis, Missouri; and Juan del Regato, M. D., Colorado Springs, Colorado.

An outstanding program has been arranged.

Special travel plans provide for departure from Los Angeles, February 4, immediately following the Annual Meeting of the American College of Radiology, and return February 11 to the West Coast gateway city of Los Angeles or San Francisco.

Further information may be obtained by writing to Hawaiian Radiological Conference, c/o Group Travel Services, Inc., 3545 Broadway, Kansas City, Missouri 64111.

BOOK REVIEW

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

Human Pathology: An Introduction to Medicine. By Robert P. Morehead, B.S., M.A., B.S.Med., M.D., F.A.C.P., F.C.A.P., Professor of Pathology and Chairman of the Department of Pathology, The Bowman Gray School of Medicine of Wake Forest College; Chief of Pathology, The North Carolina Baptist Hospital; and Pathologist to the Medical Center. Cloth. Pp. 1676, with many illustrations. Price, \$23.50. McGraw-Hill Book Company, 330 West 42nd Street, New York, N. Y., 1965.

This text of general pathology aims to provide one with a basis for understanding human disease. Dr. Morehead intended it to "serve as an introduction to the study of pathology for the second-year medical students and as a basic text for continuing study for third and fourth year medical students, house officers, and practicing physicians and surgeons." Encompassing this much material in 1676 pages is not an easy task.

Superbly illustrated and up-to-date, the text, with a rather terse didactic but readable style should succeed admirably for the medical student.

It contains, besides the usual framework of disease, several specific chapters which are unusual in textbooks on pathology. Of special interest are those on Genetics, Animal to Man Infectious Diseases, Clinicopathologic Research, and Neoplasms of Mesenchymal, Neural, and Epithelial Origin.

For the practicing physician the brevity of discussion (although presenting most diseases) precludes depth of information. For these readers, it will provide mainly a starting place in the investigation of disease.

This book will have definite usefulness and popularity as a text of general pathology among radiologists.

RICHARD C. PFISTER, M.D.

BOOKS RECEIVED

PRINCIPLES OF ENVIRONMENTAL MONITORING RE-LATED TO THE HANDLING OF RADIOACTIVE MA-TERIALS. ICRP Publication 7. A report by Committee 4 of the International Commission on Radiological Protection. Paper. Pp. 11. Price, \$1.10. Pergamon Press Inc., Long Island City, N. Y., 1966.

The Evaluation of Risks from Radiation. A report prepared for Committee 1 of the International Commission on Radiological Protection and received by the Committee on April 20th, 1965. ICRP Publication 8. Paper. Pp. 60. Price, \$2.00. Pergamon Press Inc., Long Island City, N. Y., 1966.

Pulmonary Diseases and Anomalies of Infancy AND CHILDHOOD: THEIR DIAGNOSIS AND TREAT-MENT. By Milton I. Levine, M.D., F.A.C.C.P., Attending Pediatrician, New York Hospital; Associate Professor of Clinical Pediatrics, Cornell University Medical College; Director, Pediatric Pulmonary Clinic, New York Hospital, New York; and Armond V. Mascia, M.D., F.A.C.C.P., Assistant Attending Pediatrician, New York Hospital; Assistant Professor of Clinical Pediatrics, Cornell University Medical College; Member, Pediatric Pulmonary Clinic, New York Hospital; Director, Pediatrics, Phelps Memorial Hospital, Tarrytown, N. Y. Cloth. Pp. 368, with 148 illustrations. Price, \$12.00. Hoeber Medical Division, Harper & Row Publishers, Inc., 49 East 33rd Street, New York, N. Y., 1966.

Angiographie in der Knochenpathologie. By Prof. Dr. Ludovico Mucchi, Leiter der Röntgenabteilung der Chirurgischen Universitätsklinik Mailand; Prof. Dr. Italo F. Goidanich, Direktor der Orthopädischen Universitätsklinik Pavia; and Prof. Dr. Silvio Zanoli, Assistent am Rizzoli-Institut Bologna. Cloth. Pp. 172, with 104 illustrations. Price, Ganzleinen DM 77.-. Georg Thieme Verlag, Stuttgart. In U. S. A. and Canada, Intercontinental Medical Book Corporation, New York 16, N. Y., 1966.

BILDGÜTE IN DER RADIOLOGIE. Symposion am 1. und 2. Oktober 1964 auf der Insel Herrenchiemsee/Obb. Edited by Prof. Dr. Friedrich-Ernst Stieve, München. Paper. Pp. 415, with 21 tables and 197 illustrations. Price, \$13.75. Gustav Fischer Verlag, Stuttgart. In U. S. A. and Canada, Intercontinental Medical Book Corporation, New York 16, N. Y., 1966.

Radiographic Atlas of the Genitourinary System. By Charles Ney, M.D., and Richard M. Friedenberg, M.D., with ten contributing authors. Cloth. Pp. 741, with 1,661 figures. Price, \$36.00. J. B. Lippincott Company, East Washintogn Square, Philadelphia, Pa., 1966.

THE BIOLOGICAL BASIS OF RADIATION THERAPY.

- Edited by Emanuel E. Schwartz, M.D., Director, Division of Radiation Therapy and Nuclear Medicine; Associate Professor of Radiology, School of Medicine, University of Virginia, Charlottesville, Va.; with a foreword by Juan A. del Regato, M.D. Cloth. Pp. 624, with some illustrations. Price, \$18.50. J. B. Lippincott Company, East Washington Square, Philadelphia, Pa., 1966.
- PROTECTING AND IMPROVING HEALTH THROUGH THE RADIOLOGICAL SCIENCES. Report to the Surgeon General, U. S. Public Health Service. Prepared by the National Advisory Committee on Radiation, April, 1966. Paper. Pp. 27, with some figures. U. S. Department of Health, Education, and Welfare, Public Health Service, Washington, D. C., 1966.
- HYPERBARIC OXYGEN AND RADIATION THERAPY OF CANCER. Proceedings, First Annual San Francisco Cancer Symposium. Edited by Jerome M. Vaeth, M.D., Director, Claire Zellerbach Saroni Memorial Tumor Institute of San Francisco. Paper. Pp. 284, with some illustrations. McCutchan Publishing Corporation, Berkeley, Calif., 1966.
- RADIATION PROTECTION. Recommendations of the International Commission on Radiological Protection (Adopted September 17, 1965). ICRP Publication 9. Cloth. Pp. 27. Price, \$1.75. Published for The International Commission on Radiological Protection by Pergamon Press Inc., Long Island City, N. Y., 1966.
- Manual on Environmental Monitoring in Normal Operation. Safety Series No. 16. International Atomic Energy Agency, Vienna, 1966. Paper. Pp. 70, with some figures. Price, \$1.50. International Publications, Inc., 319 East 34th Street, New York, N. Y., 1966.
- TECHNIQUES FOR CONTROLLING AIR POLLUTION FROM THE OPERATION OF NUCLEAR FACILITIES. Report of a panel on Techniques for Preventing Atmosphere Pollution from the Operation of Nuclear Facilities, Vienna, Nov. 4–8, 1963. Safety Series No. 17, International Atomic Energy Agency, Vienna, 1966. Paper. Pp. 117, with some illustrations. Price, \$2.50. International Publications, Inc., 319 East 34th Street, New York, N. Y., 1966.
- IAEA RESEARCH CONTRACTS. Sixth Annual Report.
 Technical Reports Series No. 53. International
 Atomic Energy Agency, Vienna, 1966. Paper.
 Pp. 131. Price, \$1.00. International Publications,
 Inc., 319 East 34th Street, New York, N. Y., 1966.
- THE VENTILATORY CAPACITY IN HEALTH SUBJECTS:
 AN ANALYSIS OF CAUSAL FACTORS WITH SPECIAL
 REFERENCE TO THE RESPIRATORY FORCES. By
 Torsten Ringqvist. Paper. Pp. 179. The Scandinavian Journal of Clinical & Laboratory Investigation, Volume 18, Supplementam 88. Elanders
 Boktryckeri Atkiebolag, Goteborg, Sweden, 1966.
- ACTIVATOR-FREE PORCINE PLASMIN. By C. J. Amris, Vagn Larsen, J. Brockner, and O. Storm. Paper.

- Pp. 43, with some figures. The Scandinavian Journal of Clinical & Laboratory Investigation. Volume 18, Supplementum 89. A. W. Broggers Boktrykkeri A/S, Oslo, 1966.
- LA PRATIQUE DE L'ANGIOGRAPHIE: METHODE ANATOMO CLINIQUE D'EXPLORATION DE L'APPAREIL CIRCULATOIRE ET TECHNIQUES OPERATOIRES. By E. Ecoiffier, Electroradiologiste des Hôpitaux de Paris. Paper. Pp. 288, with 114 figures. Price, 70 F. Masson & Cie, Éditeurs, 120, Boulevard Saint-Germain, Paris, 1966.
- THE RADIOLOGIC CLINICS OF NORTH AMERICA. Symposium on The Radiology of Trauma. Sidney W. Nelson, M.D., Guest Editor. Cloth. Pp. 219, with many illustrations. August, 1966, Volume IV, Number 2. W. B. Saunders Company, West Washington Square, Philadelphia, Pa., 1966.
- RADIOGRAPHIC EXAMINATION IN BLUNT ABDOMINAL TRAUMA. By James J. McCort, M.D., Director of Radiology, Santa Clara County Hospital, San Jose, Calif.; Clinical Associate Professor in Radiology, Stanford University Medical School, Palo Alto, Calif. Cloth. Pp. 252, with many illustrations. Price, \$10.50. W. B. Saunders Company, West Washington Square, Philadelphia, Pa., 1966.
- MORRIS' HUMAN ANATOMY: A COMPLETE SYSTE-MATIC TREATISE. Twelfth edition. Edited by Barry J. Anson, Ph.D., Robert Laughlin Rea, Professor, Emeritus, Department of Anatomy, Northwestern University Medical School; Research Professor, Department of Otolaryngology and Maxillofacial Surgery, College of Medicine, State University of Iowa. Cloth. Pp. 1,624, with many illustrations. Price, \$24.00. McGraw-Hill Book Company, 330 West 42nd Street, New York, N. Y., 1966.
- THE RADIOCHEMICAL MANUAL. Second edition. Edited by B. J. Wilson. Cloth. Pp. 328, with many charts. Price, 50s. The Radiochemical Centre, Amersham, Buckinghamshire, England, 1966.
- ROENTGEN SIGNS IN CLINICAL PRACTICE. In two volumes. By Isadore Meschan, M.A., M.D., Professor and Director of the Department of Radiology, The Bowman Gray School of Medicine of Wake Forest College, Winston-Salem N. C.; Formerly Professor and Head, Department of Radiology, University of Arkansas School of Medicine, Little Rock, Ark.; with the assistance of R. M. F. Farrer-Meschan, M.B., B.S., (Melbourne, Australia), M.D., Research Associate, Department of Radiology, The Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C. Volume I, Basic Principles and Radiology of the Skeletal System. Volume II, Radiology of the Chest, Genitourinary System and Gastrointestinal Tract. Cloth. Pp. Volume I, 1 to 718-Volume II, 719 to 1831, with many illustrations. Price, \$38.∞ for the set of two Volumes, W. B. Saunders Company, West Washington Square, Philadelphia, Pa., 1966.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

United States of America

AMERICAN ROENTGEN RAY SOCIETY

Secretary, Dr. C. Allen Good, Mayo Clinic, Rochester, Minn. Annual meeting: San Francisco Hilton Hotel, San Francisco, Calif., Sept. 27-30, 1966.

AMERICAN RADIUM SOCIETY

Secretary, Dr. Fernando G. Bloedorn, Division of Radiotherapy, University of Maryland Hosp., Baltimore, Md. 21201. Annual meeting: Royal York Hotel, Toronto, Ont., Canada, May 29-31, 1967. RADIOLOGICAL SOCIETY OF NORTH AMERICA

Secretary-Treasurer, Dr. Maurice Doyle Frazer, 1744 South Fifty-eighth St., Lincoln, Neb. Annual meeting: Palmer House, Chicago, Ill., Nov. 27–Dec. 2, 1966.

AMERICAN COLLEGE OF RADIOLOGY

Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Ill. Annual meeting: Century Plaza Hotel, Los Angeles, Calif., Jan. 31-Feb. 4, 1967.

Section on Radiology, American Medical Association Secretary, Dr. Kenneth L. Krabbenhoft, Harper Hospital, Detroit, Mich. 48201. Annual meeting: Atlantic City, June 18-22, 1967.

AMERICAN BOARD OF RADIOLOGY

Secretary, Dr. H. Dabney Kerr. Correspondence should be directed to Kahler Hotel Building, Rochester, Minn. The Fall 1966 examination will be held at the Washington Hilton Hotel. Washington, D.C., December 5-9, inclusive. The deadline for filing applications was June

30, 1966.
The Spring 1967 examination will be held at the Pittsburgh Hilton Hotel, Pittsburgh, Pennsylvania, June 5–9, inclusive. The deadline for filing applications for this

examination is December 31, 1966

The Fall 1967 examination will be held at the Statler Hilton Hotel, Dallas, Texas, December 4-8, inclusive. The deadline for filing applications is June 30, 1967.

AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE Secretary, Leonard Stanton, Hahnemann Medical College, 230 N. Broad St., Philadelphia, Pa. 19102. Annual meeting to be announced.

AMERICAN CLUB OF THERAPEUTIC RADIOLOGISTS Secretary, Dr. J. A. del Regato, Penrose Cancer Hospital, Colorado Springs, Colo.

TWELFTH INTERNATIONAL CONGRESS OF RADIOLOGY President, Dr. Kempo Tsukamoto, 9-1, 4-chome, Angewa, Chiba, Japan. Meeting: Hotel New Otane, Tokyo, Japan, Oct. 6-11, 1969.

NINTH INTER-AMERICAN CONGRESS OF RADIOLOGY Counselor for the United States, Dr. Philip J. Hodes, Jefferson Medical College Hospital, 11th and Walnut Streets, Philadelphia 7, Pennsylvania.

President, Dr. Leandro Zubiaurre, Montevideo, Uruguay. Meeting: Hotel San Rafael, Punta-del Este, Uruguay,

Nov. 29-Dec. 5, 1967. INTER-AMERICAN COLLEGE OF RADIOLOGY

President, Dr. Oscar Soto, H. Urteaga 480, Lima, Perú.

ALABAMA RADIOLOGICAL SOCIETY

Secretary, Dr. Walter Brower, Birmingham, Ala. Meets time and place of Alabama State Medical Association.

AMERICAN NUCLEAR SOCIETY

Treasurer, Raymond Maxson, 86 E. Randolph St., Chicago, Ill. Annual meeting to be announced.

American Society for Diagnostic Ultrasound Secretary, Dr. Charles C. Grossman, 552 N. Neville St., Pittsburgh, Pa. 15213.

Arizona Radiological Society

Secretary-Treasurer, Dr. George Gentner, 3435 W. Durango, Phoenix, Ariz. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

ARKANSAS CHAPTER OF AMERICAN COLLEGE OF RADIOLOGY Secretary-Treasurer, Dr. William J. Rhinehart, St. Vin-

cent Infirmary, Little Rock, Ark. 72205.

ARKANSAS RADIOLOGICAL SOCIETY Secretary, Dr. Charles W. Anderson, 11082 Poplar, Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Association of University Radiologists Secretary-Treasurer, Dr. Stanley Rogoff, Department of Radiology, University of Rochester Medical School, Rochester, New York 14620. Annual meeting: Temple University School of Medicine, Philadelphia, Pa., May

12-13, 1967.

ATLANTA RADIOLOGICAL SOCIETY

Secretary, Dr. Donald R. Rooney, Burnt Hickory Road, Marietta, Ga. Meets monthly except during three summer months, on third Tuesday, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

BAVARIAN-AMERICAN RADIOLOGIC SOCIETY Secretary, Colonel Kurt Harrell, Landstuhl Army Medical Center, Landstuhl, Germany. Meets quarterly.

BLOCKLEY RADIOLOGICAL SOCIETY Secretary-Treasurer, Dr. R. John Gould, 441 Lombardy Rd., Drexel Hill, Pa. 19026.

BLUEGRASS RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Arthur Lieber, University of Kentucky, University Hospital, Lexington, Kentucky. Meets quarterly.

Brooklyn Radiological Society

Secretary, Dr. Robert L. Pinck, Long Island College Hospital, 340 Henry St., Brooklyn, N. Y. Meets first Thursday of each month, October through June.

BUFFALO RADIOLOGICAL SOCIETY

Secretary, Dr. Victor A. Panaro, 42 Burroughs Drive, Buffalo, N.Y. 14226. Meets second Monday evening each month, October to May inclusive.

CALIFORNIA RADIOLOGICAL SOCIETY

Secretary, Dr. L. Henry Garland, Suite 1739, 450 Sutter St., San Francisco, Calif. Meets annually during meeting of California Medical Association.

CATAWBA VALLEY RADIOLOGICAL SOCIETY

Secretary, Dr. Emmett R. White, P. O. Box 303, Rutherford College, N. C. Meets every Tuesday, Dept. of Radiology, Valdese General Hosp., Valdese, N. C., at 12:00 P.M.

CENTRAL NEW YORK RADIOLOGICAL SOCIETY Secretary-Treasurer, Dr. Robert A. Bornhurst, State Univ. Hospital, 750 E. Adams St., Syracuse, N. Y. 13210. Meets first Monday each month, October through May.

CENTRAL OHIO RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Atis K. Freimanis, Ohio State Univ. Hospitals, 410 W. 10th Ave., Columbus, Ohio 43210. Meets second Thursday in October, November, January, and March 15 and May 19 at Fort Hayes Hotel, Columbus, Ohio.

Central Society of Nuclear Medicine

Secretary, Dr. Robert S. Landauer, Radiation Center Bldg., 1903 West Harrison St., Chicago 12, Ill.

CHICAGO ROENTGEN SOCIETY

Secretary-Treasurer, Dr. Fredric D. Lake, 2548 N. Lake-

^{*} Secretaries of societies are requested to send timely information promptly to the Editor.

view Ave., Chicago, Ill. 60614. Meets second Thursday of each month, October to April, except December, at the Pick-Congress Hotel at 8:00 P.M.

CLEVELAND RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. James Christie, 10515 Carnegie Avenue, Cleveland, Ohio. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

COLORADO RADIOLOGICAL SOCIETY

Secretary, Dr. George F. Wertz, 1801 High St., Denver, Colo. Meets third Friday of each month at Denver Athletic Club from September through May.

CONNECTICUT VALLEY RADIOLOGIC SOCIETY

Secretary, Dr. William W. Walthall, Jr., 130 Maple St., Springfield, Mass. Meets in April and October.

Dallas-Fort Worth Radiological Society
Secretary-Treasurer, John S. Alexander, 1217 W. Cannon,

Ft. Worth, Tex. Meets monthly, third Monday, at Southwest International Airport at 6:30 P.M.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY

Secretary, Dr. Robert L. Willis, Harper Hospital, Detroit , Mich. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

EAST BAY RADIOLOGICAL SOCIETY

Secretary, Dr. Tom H. Piatt, 12 Camino Encinas, Orinda, Calif. 94563. Meets first Thursday each month, Oct. through May, at University Club, Oakland, Calif.

EAST TENNESSEE RADIOLOGICAL SOCIETY

Secretary, Dr. C. H. Kimball, 2200 Harris Circle, Cleveland, Tenn. Meets in January and September.

EASTERN RADIOLOGICAL SOCIETY

Secretary, Dr. James F. Martin, North Carolina Baptist Hospital, Winston-Salem, N. C.

FLORIDA RADIOLOGICAL SOCIETY

Secretary, Dr. John C. Jowett, Orlando, Fla. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

FLORIDA WEST COAST RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Garth R. Drewry, Tampa General Hospital, Tampa 6, Fla. Meets in January, April, July and October.

GEORGIA RADIOLOGICAL SOCIETY

Secretary, Dr. Al Rayle, Jr., 938 Peachtree St., N. E., Atlanta, Ga. Meets in spring and fall with Annual State Society Meeting.

GREATER MIAMI RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Arthur R. Miller, North Miami General Hospital, 1701 N.E. 127th St., North Miami, Fla. Meets monthly, third Wednesday at 8:00 P.M., at Jackson Memorial Hospital, Miami, Fla.

GREATER ST. LOUIS SOCIETY OF RADIOLOGISTS

Secretary-Treasurer, John W. Fries, 3520 Chippewa St., St. Louis, Mo. 63118.

HAWAII RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Donald Ikeda, Kuakini Hospital, 347 N. Kuakini St., Honolulu, Hawaii 96817. Meets third Monday of each month at 7:30 P.M.

HOUSTON RADIOLOGICAL SOCIETY

Secretary, Dr. William A. Vint, 1004 Seymour, Pasadena, Tex. Meets fourth Monday of each month, except June, July, August and December, at the Doctors' Club, 8:00 P.M., Houston, Tex.

IDAHO STATE RADIOLOGICAL SOCIETY

Secretary, Dr. George H. Harris, Bannock Memorial Hospital, Pocatello, Idaho. Meets in the spring and fall.

Illinois Radiological Societ

Secretary, Dr. George A. Miller, Carle Hospital Clinic, Urbana, Ill. Meets in the spring and fall.

INDIANA ROENTGEN SOCIETY, INC.

Secretary, Dr. Richard A. Silver, 1815 N. Capitol Avenue, Indianapolis, Ind. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

IOWA RADIOLOGICAL SOCIETY

Secretary, Dr. L. L. Maher, 1419 Woodland Ave., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

KANSAS RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Robert C. Lawson, 310 Medical Arts Bldg., 10th and Horne, Topeka, Kan. Meets in spring with State Medical Society and in winter on call.

Kentucky Chapter, American College of Radiology Secretary-Treasurer, Dr. Robert H. Greenlaw, Dept. of Radiology, Univ. of Kentucky Med. Ctr., Lexington, Ky. Meets semiannually.

KENTUCKY RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Joan R. Hale, 402 Heyburn Building, Louisville, Ky. Meets monthly on second Friday at Sheraton Hotel, Louisville, Ky.

KINGS COUNTY RADIOLOGICAL SOCIETY

Secretary, Dr. Sidney Hendler, 1880 Ocean Ave., Brooklyn 30, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

KNOXVILLE RADIOLOGICAL SOCIETY

Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

LONG ISLAND RADIOLOGICAL SOCIETY

Secretary, Dr. Samuel Gelband. Meets second Tuesday of the month in February, April, June, October and December.

Los Angeles Radiological Society

Secretary, Dr. Norman Zheutlin, 8720 Beverly Blvd., Los Angeles, Calif. Meets second Wednesday of month in September, November, January, April and June at Los Angeles County Medical Association Building, Los Angeles, Calif.

LOUISIANA-TEXAS GULF COAST RADIOLOGICAL SOCIETY Secretary-Treasurer, Dr. Edward A. Sheldon, 109 Doctors

Bldg., Beaumont, Texas 77701. Maine Radiological Society

Secretary, Dr. J. T. Chen, 7 Cherry Hill Terrace, Waterville, Me. Meets in June, September, December and April

MARYLAND RADIOLOGICAL SOCIETY

Secretary, Dr. Henry Startzman, Medical Arts Building, Baltimore, Md.

MEMPHIS ROENTGEN SOCIETY

Secretary-Treasurer, Dr. Vernon I. Smith, Jr., Suite 203, 1085 Madison Ave., Memphis, Tenn. 38104. Meets first Monday of each month at John Gaston Hospital.

MIAMI VALLEY RADIOLOGICAL SOCIETY

Secretary, Dr. Darwood B. Hance, Reid Memorial Hospital, Richmond, Indiana. Meets third Thursday of fall, winter and spring months at 7:30 P.M. at Miami Valley Hospital, Dayton, Ohio.

MID-HUDSON RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Alexander W. Friedman, Mid-Hudson Medical Group, Fishkill, N. Y. Meets 7:00 P.M., first Wednesday of each month, September to May.

MILWAUKEE ROENTGEN RAY SOCIETY

Secretary-Treasurer, Dr. Donald P. Babbitt, 1700 W. Wisconsin Ave., Milwaukee, Wis. 53233. Meets monthly on fourth Monday, October through May, at University Club.

MINNESOTA RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Edward A. Peterson, 572 Lowry Medical Arts Bldg., St. Paul, Minn. Meets twice annually, fall and winter.

MISSISSIPPI RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Dan T. Keel, Jr., 504 Chippewa St., Brookhaven, Miss. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 P.M.

MISSOURI RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. M. Shoss, Cape Girardeau, Mo. MONTANA RADIOLOGICAL SOCIETY

Secretary, Dr. Clark Grimm, Great Falls, Montana. Meets at least once a year.

NEBRASKA STATE RADIOLOGICAL SOCIETY

Secretary, Dr. Richard Bunting, The Radiologic Center, Nebraska Methodist Hospital, Omaha 31, Neb. Meets third Wednesday of each month at 6 p.m. in Omaha or Lincoln.

NEVADA RADIOLOGICAL SOCIETY

Secretary, Dr. William G. Arbonies, Department of Radiology, St. Mary's Hospital, Reno, Nev.

New England Roentgen Ray Society

Secretary, Dr. Jack R. Dreyfuss, Zero Emerson Place, Boston, Mass. 02114. Meets third Friday of each month, October through May, at The Longwood Towers, 20 Chapel Street, Brookline, Mass., at 4:30 P.M.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY

Secretary, Dr. Paul Y. Hasserjian, 1470 Elm St., Manchester, N. H. Meets four to six times yearly.

New Mexico Association of Radiologists

Secretary-Treasurer, Dr. Justin J. Wolfson, Department of Radiology, Bernalillo County-Indian Hospital, Albuquerque, New Mexico.

NEW MEXICO SOCIETY OF RADIOLOGISTS

Secretary, Dr. William G. McPheron, Hobbs, New Mexico. Four meetings annually, three held in Albuquerque, N. M., and one held at time and place of New Mexico State Medical Society annual meeting.

NEW YORK ROENTGEN SOCIETY

Secretary, Dr. Milton Elkin, Albert Einstein College of Medicine, Bronx, N.Y. 10461. Meets monthly on third Monday at the New York Academy of Medicine at 4:30 P.M. Annual meeting to be announced.

NORTH CAROLINA RADIOLOGICAL SOCIETY

Secretary, Dr. E. H. Schultz, North Carolina Memorial Hospital, Chapel Hill, N. C. Meets in the spring and fall each year.

North Dakota Radiological Society

Secretary, Dr. Robert J. Olson, 1240 8th Ave., Williston, N. D. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

NORTH FLORIDA RADIOLOGICAL SOCIETY

Secretary, Dr. Charles H. Newell, 800 Miami Road, Jacksonville 7, Fla. Meets quarterly in March, June, September and December.

Northeastern New York Radiological Society Secretary, Dr. Anthony J. Tabacco, 621 Central Ave., Albany 6, N. Y. Meets in Albany area on second Wednesday of October, November, March and April.

NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY Secretary-Treasurer, Dr. John Turner, 1215-28th St., Sacramento, Calif. Meets fourth Monday of Sept., Nov., Jan., March and May at the Sutter Club in Sacramento. Northwestern Ohio Radiological Society

Secretary, Dr. Vito J. Zupa, Mercy Hospital, Department of Radiology, Toledo, Ohio.

OHIO STATE RADIOLOGICAL SOCIETY

Secretary, Dr. Mortimer Lubert, Mt. Sinai Hospital, Cleveland, Ohio. Annual meeting to be announced.

OKLAHOMA STATE RADIOLOGICAL SOCIETY

Secretary, Dr. Robert Sukman, 1200 N. Walker, Oklahoma City, Okla. Meets in January, May and October.

ORANGE COUNTY RADIOLOGICAL SOCIETY Secretary, Dr. George W. Logan, 301 Newport Blvd., Newport Beach, Calif. Meets fourth Tuesday of every month at Orange County Medical Association Build-

Oregon Radiological Society

Secretary-Treasurer, Dr. Robert S. Miller, 13753 S.W. Farmington Rd., Beaverton, Ore. 97005. Meets on second Wednesday of month, October through April, at the University Club, Portland, Ore.

Orleans Parish Radiological Society

Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets second Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Willis Taylor, 1118 9th Ave., Seattle, Washington. Annual meeting to be announced. PENNSYLVANIA RADIOLOGICAL SOCIETY

Secretary, Dr. T. Frederick Weiland, 619 Ridgeway Ave., Grove City, Pa. Annual meeting to be announced.

PHILADELPHIA ROENTGEN RAY SOCIETY Secretary, Dr. C. Jules Rominger, Misericordia Hospital, 54th St. and Cedar Ave., Philadelphia, Pa. 19143. Meets first Thursday of each month at 5 P.M., from October to May in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY Secretary, Dr. Robert N. Berk, 9100 Babcock Blvd., Pittsburgh, Pa. 15237. Meets second Wednesday of month, October through June, at Park Schenley Restaurant.

RADIOLOGICAL SOCIETY OF CONNECTICUT, INC. Secretary-Treasurer, Dr. Orlando F. Gabriele, 1450 Chapel St., New Haven 11, Conn. Meetings are held quarterly.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI Secretary, Dr. Harold N. Margolin, 6159 Tulane Road, Cincinnati, Ohio. Meets first Monday of each month at

Cincinnati Academy of Medicine.

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY Secretary, Dr. J. Stewart Whitmore, 1010 Rialto Bldg., Kansas City, Mo. Meets last Friday of each month. RADIOLOGICAL SOCIETY OF KANSAS CITY

Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

RADIOLOGICAL SOCIETY OF LOUISIANA
Secretary, Dr. Lester W. Eavenson, 2700 Napoleon Ave., New Orleans 15, La. Meets semiannually, during Louisiana State Medical Society meeting and 6 months later.

RADIOLOGICAL SOCIETY OF NEW JERSEY Secretary, Dr. John W. Marquis, 12 Hawthorne Ave., East Orange, N. J. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

RADIOLOGICAL SOCIETY OF RHODE ISLAND Secretary-Treasurer, Dr. John M. Vesey, 1196 Elmwood Ave., Cranston, R. I.

RADIOLOGICAL SOCIETY OF SOUTH DAKOTA Secretary-Treasurer, Dr. Donald J. Peik, 303 S. Minnesota Ave., Sioux Falls, S. D.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA Secretary-Treasurer, Dr. Gerald M. McDonnel, U.C.L.A. Medical Center for Health Sciences, Los Angeles, Calif. 90024. Meets three times a year, usually October, February and May,

RADIOLOGICAL SOCIETY OF THE STATE OF NEW YORK Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester 18, N. Y.

REDWOOD EMPIRE RADIOLOGICAL SOCIETY Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

RICHMOND COUNTY RADIOLOGICAL SOCIETY Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y. Secretary, Dr. Irving B. Joffe, Rochester General Hospital, 1425 Portland Ave., Rochester 21, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY Secretary-Treasurer, Dr. Robert W. Lackey, 4200 E. Ninth Ave., Denver, Colo. Annual meeting to be announced.

SAN ANTONIO-MILITARY RADIOLOGICAL SOCIETY Secretary, Dr. Hugho F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Tex. Meets third Wednesday of each month in Fort Sam Houston Officer's Club at 6:30 P.M.

SAN DIEGO RADIOLOGICAL SOCIETY President-Secretary, Charles P. Hyslop, 7901 Frost St., San Diego 22, Calif. Meets first Wednesday of each month at the University Club.

SAN FRANCISCO RADIOLOGICAL SOCIETY Secretary, Dr. H. Joachim Burhenne, Children's Hospital and Adult Medical Center, 3700 California St., San Francisco, Calif. 94119. Meets quarterly at the San Francisco Medical Society, 250 Masonic Ave., San Francisco, Calif. 94118.

SANTA CLARA COUNTY RADIOLOGICAL SOCIETY Secretary, Dr. Bill G. Karras. Meets monthly at the Santa Clara County Medical Association Bldg., 700 Empey Way, San Jose, Calif.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

Section on Radiology, Medical Society of the District of Columbia Secretary-Treasurer, Dr. Gregory T. Henesy, 915 19th St., N. W., Washington, D. C. 20006. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section on Radiology, Southern Medical Association Secretary, Dr. Andrew F. Giesen, Jr., White-Wilson Clinic, Fort Walton Beach, Fla. Annual meeting: Washington, D. C., Nov. 14-17, 1966.

Section on Radiology, Texas Medical Association Secretary, Dr. George F. Crawford, St. Elizabeth Hospital, Beaumont, Tex. Meets annually with the Texas Medical Association.

SHREVEPORT RADIOLOGICAL CLUB Secretary, Dr. W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

SOCIETY FOR PEDIATRIC RADIOLOGY

Secretary, Dr. John L. Gwinn, Children's Hospital, 4614 Sunset Blvd., Los Angeles 27, Calif. Annual meeting: Washington Hilton Hotel, Washington, D. C., Sept. 25, 1967.

Society of Nuclear Medicine
Secretary, Mr. C. Craig Harris, Oak Ridge National
Laboratories, Oak Ridge, Tenn. Administrator, Mr.
Samuel N. Turiel, 430 N. Michigan Ave., Chicago 11, Ill.
Annual meeting to be announced.

SOUTH BAY RADIOLOGICAL SOCIETY

Secretary, Northern Section: Dr. John H. Callaghan, 2900 Whipple Ave., Redwood City, Calif.; Southern Sec-tion: Dr. Carleton J. Wright, 2015 Clarman Way, San Jose, Calif. Meets second Wednesday of each month.

South Carolina Radiological Society

Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

SOUTH DAKOTA RADIOLOGICAL SOCIETY

Secretary, Dr. Donald J. Peik, 1417 S. Minnesota Ave. Sioux Falls, S. Dak. Meets in spring with State Medical Society and in fall.

SOUTHERN RADIOLOGICAL CONFERENCE

Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 4097, Mobile, Ala. Annual meeting to be announced.

SOUTHWESTERN RADIOLOGICAL SOCIETY

Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

TENNESSEE RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. E. K. Carter, Holston Valley Community Hosp., Kingsport, Tenn. Meets annually at the time and place of the Tennessee State Medical Association meeting.

Texas Radiological Society

Secretary, Dr. Herman C. Sehested, 815 Medical Arts Bldg., Fort Worth 2, Tex. Annual meeting to be announced.

TRI-STATE RADIOLOGICAL SOCIETY

Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:∞ P.M., Elks Club in Evansville, Ind.

University of Michigan Department of Roentgen-OLOGY STAFF MEETING

Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital, Ann Arbor, Mich.

UPPER PENINSULA RADIOLOGICAL SOCIETY Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

UTAH STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Carlisle C. Smith, Salt Lake General Hospital, 2033 S. State St., Salt Lake City, Utah. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

VERMONT RADIOLOGICAL SOCIETY
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VIRGINIA RADIOLOGICAL SOCIETY

Secretary, Dr. John M. Ratliff, Mary Immaculate Hospital, Newport News, Va.

Washington State Radiological Society

Secretary, Dr. Owen Marten, 930 Terry Avenue, Seattle, Wash. Meets quarterly.

WEST VIRGINIA RADIOLOGICAL SOCIETY

Secretary, Dr. Karl J. Myers, The Myers Clinic-Broad-dus Hospital, Philippi, W. Va. Meets concurrently with Annual Meeting of West Virginia State Medical Society; other meetings arranged by program committee.

WESTCHESTER COUNTY RADIOLOGICAL SOCIETY

Secretary, Dr. Arnold Gerson, Medical Arts Bldg., Mt. Vernon, N. Y. Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society

Secretary-Treasurer, Harold F. Ibach, 2400 W. Villard Ave., Milwaukee, Wis. Meets twice a year, May and September.

WYOMING RADIOLOGICAL SOCIETY

Secretary, Dr. Ronald R. Lund, 240 W. 9th St., Casper, Wyo. Meets in Bl. with State Medical Society and in spring on call of President.

Cuba, Mexico, Puerto Rico and Central America

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Sociedad de Radiología y Fisioterapía Cubana Secretary, Dr. Miguel A. García Plasencia, Hospital Curie, 29 y F, Vedado, Habana, Cuba. Meets monthly at Curie Hospital.

Sociedad Costarricense de Radiologia

Secretary, Dr. James Fernández Carballo, Apartado VIII, San José, Costa Rica.

Sociedad Mexicana de Radiología, A.C. Coahuila No. 35, México 7, D. F. Secretary-General, Dr. Armando L. Rodríguez Meets first Monday of each month.

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Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting. Sociedad Radiológica de Puerto Rico

Secretary, Dr. José T. Medina, Apt. 9387, Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

British Commonwealth of Nations

Association of Radiologists of the Province of Quebec Secretary, Dr. R. Robillard, Notre-Dame Hospital, 1560 Sherbrooke St., East, Montreal, Que., Canada. Meets four times a year.

BRITISH INSTITUTE OF RADIOLOGY

Honorary Secretary, Dr. G. H. du Boulay, 32 Welbeck St., London, W. I, England. Meets monthly from October until May. Annual meeting: Central Hall and Caxton Hall, Westminster, London, S. W. 1., England, April 26-28, 1967

CANADIAN ASSOCIATION OF PHYSICISTS, DIVISION OF MEDICAL AND BIOLOGICAL PHYSICS

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EDMONTON AND DISTRICT RADIOLOGICAL SOCIETY
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various Edmonton Hospitals. FACULTY OF RADIOLOGISTS

Honorary Secretary, Dr. J. N. Pattinson, 47 Lincoln's Inn Fields, London, W.C.2, England. Annual meeting to be announced.

FACULTY OF RADIOLOGISTS, ROYAL COLLEGE OF SURGEONS IN IRELAND

Registrar, Dr. H. O'Flanagan, F.R.C.P.I., D.P.H., 123 St. Stephens Green, Dublin 2, Ireland.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDI-CINE (CONFINED TO MEDICAL MEMBERS)

Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, I Wimpole St., London, W. I, Eng-

Canadian Association of Radiologists

Honorary Secretary-Treasurer, Dr. Maurice Dufresne, Associate Honorary Secretary-Treasurer, Dr. F. Robert MacDonald, 1555 Summerhill Ave., Montreal 25, Que., Canada. Annual meeting to be announced.

MONTREAL RADIOLOGICAL STUDY CLUB

Secretary, Dr. Leonard Rosenthall, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday

evening, October to April.

Section of Radiology, Canadian Medical Association Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française de Radiologie Secretary General, Dr. Jacques Lespérance, 5415 Boul. L'Assomption, Montreal 26, P. Q., Canada. Meets every third Tuesday from October to April. Annual meeting: Dec. 8-10, 1966.

TORONTO RADIOLOGICAL SOCIETY

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COLLEGE OF RADIOLOGISTS OF AUSTRALASIA

Honorary Secretary, Dr. E. A. Booth, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W., Australia.

SOUTH AMERICA

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Ateneo de Radiologia

Secretary, Dr. Victor A. Añaños, Instituto de Radiologia, Santa Fe 3100, Rosario, Argentina. Meets monthly on second and fourth Fridays at 7:00 P.M. in the Hospital Nacional de Centenario, Santa Fe 1300, Rosario.

Colégio Brasileiro de Radiologia

Secretary-General, Dr. Miguel Mario Céntola, Caixa Postal 5984, São Paulo, Brazil.

Sociedad Argentina de Radiologia

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Secretary, Dr. Héctor Fernández Ferrufino, Casilla 1192, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia

Secretary, Dr. Nicola Caminha, Av. Mem. de Sa, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia

Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología

Secretary, Dr. Patricio Barriga, Casilla 13426, Santiago, Chile. Meets fourth Friday of each month.

Sociedad Colombiana de Radiologia

Secretary-General, Dr. Armando Uribe, Hospital Militar Central, Apartado aéreo No. 5804, Bogotá, Colombia. Meets last Thursday of each month.

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Sociedad Paraguaya de Radiología

Secretary, Dr. Miguel González Addone, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia

Secretary-General, Dr. Augusto Cáceres G. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta 218, Lima.

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1464, piso 13, Montevideo, Uruguay. Sociedad de Radiología de El Salvador

Secretary, Dr. Julio Astacio, 5a Av. Nte. No. 434, San Salvador, Rep. El Salvador.

Sociedade de Radiología de Pernambuco

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Paz. 151, Córdoba, Argentina. Sociedad Venezolana de Radiología

Secretary-General, Dr. Luis F. Muro, Apartado No. 9362 Candelaria, Caracas, Venezuela. Meets monthly, third Friday at Colegio Médico del Distrito Federal, Caracas.

CONTINENTAL EUROPE

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President, Dr. Konrad Weiss, Mariannengasse 10, Vienna Austria. Meets second Tuesday of each month in Allgemeine Poliklinik. Annual meeting to be announced.

Société Belge de Radiologie

General Secretary, Prof. Simon Masy, Louvain, Belgium. Meets in February, March, May, June, September, October, November and December.

Société Européenne de Radiologie Pédiatrique Permanent Secretary, Dr. Jaques Sauvegrain, Hôpital des Enfants-Malades, 149, rue de Sèvres, Paris 15e, France. General Secretary, Dr. Ole Eklöf, P.O. Box, Stockholm 60,

Sweden. Annual meeting to be announced.

Société Française d'Électroradiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, du Nord, de L'Ouest, de l'Est, et d'Alger et d'Afrique du Nord. Central Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.

Secretary-General, Dr. Ch. Proux, 9 rue Daru, Paris 8º,

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Secretary, Dr. Robert Poch, Praha 12, Srobárova 50, Czechoslovakia. Meets monthly except during July, August and September. Annual general meeting. Deutsche Röntgengesellschaf

Secretary, Professor Dr. med. H. Lossen, Universitäts-Röntgeninstitut, Lagenbeckstr. 1, Mainz, Germany. Società Italiana di Radiologia Medica e di Medicina

Nucleare

Secretary, Dr. Ettore Conte, Ospedale Mauriziano, Torino, Italy. Meets annually.

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Secretary-General, Dr. C-E. Unnérus, Hagalund-Tapiola, Havsvindsvägen 5 C., Finland. Annual meeting: Umeå,

Sweden, 1967; Copenhagen, Denmark, 1968. Sociedad Española de Radiología y Electrología

MÉDICAS Y MEDICINA NUCLEAR

Secretary, Juan Gomez Lopez, Villanueva, 11, Madrid 1. Meets every second Friday of each month, Oct. to June, inclusive, in Madrid. Annual general meeting to be announced.

Schweizerische Gesellschaft für Radiologie und NUKLEARMEDIZIN (SOCIÉTÉ SUISSE DE RADIOLOGIE ET DE MÉDECINE NUCLÉAIRE)

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Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

INDONESIAN RADIOLOGICAL SOCIETY

Secretary, Professor Sjahriar Rasad, Taman Tjut Mutiah 1, Diakarta, Indonesia.

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ROENTGEN DIAGNOSIS Head

DILENGE, D., METZGER, J., and SIMON, J. Le canal optique en neuroradiologie. (The optic canal in neuroradiology.) J. de radiol., d'électrol. et de méd. nucléaire, Nov., 1965, 46, 721-734. (From: Service de Neuroradiologie de la Pitié, Paris, France.)

The axis of the optic canal may vary in direction, not only from one patient to another according to sex and age, but also in the same subject from one side to the other. Its diameter and morphology also vary in the different segments of the same canal. In the classic incidence of Hartmann, the canal appears as a regular circle of uniform thickness, and is projected in the lower lateral quadrant of the orbit. In order to be perfect, this incidence requires that the central ray and the axis of the canal be parallel. In Reese's incidence, the optic canal is projected slightly laterally to the orbital center. This projection is more suitable for the study of the orbital apex. Tomography in Hirtz's position provides comparative study of the canal of both sides on the same film and the detection of an eventual involvement of its anterior or orbital portion, or its posterior intracranial portion. In this projection, the canal is funnel-shaped, its posterior portion being wider than the anterior one. If tomography is performed in the Hartmann incidence, the posterior section of the optic canal is oval, with transverse long axis, and its anterior section is also oval but with vertical long axis.

Study of the optic canal is indicated not only in visual syndromes, but also in certain involvements of the base of the skull, as follows:

- (1) Chiasmatic glioma: bilateral enlargement, with thinning and demineralization of the walls (70 per cent of cases). In the case of a glioma of the optic nerve, changes are similar but unilateral.
- (2) Increased intracranial pressure: widening of the canal with minimal demineralization; rarely encountered; may involve one side only.
- (3) Pituitary adenoma: the destruction of the canal is restricted to the inferior quadrant (60 per cent of cases). It may be bilateral or unilateral, and the degree of alteration of the visual field is proportional to the destruction of the optic canal.
- (4) Aneurysms: in 12 cases, changes were identical with those of pituitary adenoma, but the upper rim of the canal remained regular, and the pituitary fossa was asymmetrically eroded.
- (5) Ethmoido-sphenoid mucocele: in 3 observed cases, the orbital apex showed a lacuna with a polycyclic contour, and the lower half of the optic canal was destroyed.
- (6) Subfrontal tumors (glioma, meningioma): in

- these cases, an important decalcification of the upper border of the optic canal was observed.
- (7) Meningiomas of the orbital apex: in 1 case, the optic canal was enlarged; this is rare, usually the canal is narrowed by bony condensation. These suprasellar tumors always produce a thinning of the dorsum and sometimes an enlargement of the sella turcica. Narrowing of the optic canal was also observed in Crouzon's disease, in Paget's disease (3 cases out of 40), in craniostenosis (nearly all cases), and in osteopetrosis (2 cases).
- (8) Ethmoido-sphenoidal carcinomas: the wall of the optic canal may be completely destroyed, osteolysis involving the lower portion at the start. The floor of the sella turcica is demineralized, and the sphenoid sinus is opaque.
- (9) Hand-Schüller-Christian syndrome: when the orbit is involved, the optic canal is completely destroyed although the visual field remains intact.—H. P. Lévesque, M.D.

Hastings-James, R. Orbital pneumography. J. Canad. A. Radiologists, March, 1966, 17, 10–15. (From: Victoria General Hospital, Halifax, Nova Scotia, Canada.)

The author describes his experience with orbital pneumography in 12 patients with unilateral proptosis. Ten cc. of air is injected through a needle into the area of the muscle cone behind the globe, and an additional 2 cc. of air is introduced outside the muscle cone as the needle is withdrawn. With this technique the central surgical space of the orbit is filled, and in two-thirds of the cases air enters the capsule of Tenon to give a clear outline of the globe. Tomograms are made in the posteroanterior, oblique, and lateral projections.

In 6 cases the study was nondiagnostic or the patient's orbit was not surgically explored because of clinical considerations. In the remaining 6 patients, a tumor was demonstrated on pneumography and confirmed at surgery. These included lacrimal gland and optic nerve tumors, dermoid cysts, meningioma and carcinoma of the ethmoid.

The advantages of orbital pneumography include direct visualization of a tumor so that a roentgenologic diagnosis may be suggested and localization for surgical exploration defined. The negative findings may obviate surgical exploration and allow conservative treatment.—E. A. Franken, Jr., M.D.

Ross, Ronald J., and Greitz, Torgny V. B. Changes of the sella turcica in chromophobic adenomas and eosinophilic adenomas. *Radiology*, May, 1966, 86, 892–899. (Address: Forest City Hospital, 701 Parkwood Drive, Cleveland, Ohio.)

The increase in therapeutic modalities for the various lesions in the intrasellar and suprasellar areas

necessitates an accurate differential diagnosis. This should be made as far as possible by the plain skull film examination; consequently, the authors undertook the evaluation of the osseous changes on the plain roentgenograms in and about the sella turcica in chromophobe adenomas and eosinophilic adenomas. The primary aim was to compare the classical changes in each of these pituitary tumors in surgically and pathologically verified material.

A considerable amount has been written about the roentgenographic changes in pituitary neoplasms. It is usually agreed that the osseous changes of suprasellar tumors can be distinguished from intrasellar lesions, but this is not true for the different types of intrasellar tumors. According to the "classical" description the sella of the eosinophilic adenoma is typically balloon-shaped, indicating that the sellar entrance is either minimally widened or not at all. The angle between the planum sphenoidale and the anterior wall of the sella is acute, and the dorsum sellae is not tilted backward or significantly eroded. The sella of the chromophobic adenoma is cupshaped and the angle between the planum and the anterior sellar wall is obtuse. The sellar entrance is widened due to the backward tilt of the dorsum sellae, which is usually eroded. The sella is often asymmetric and larger than in the eosinophilic lesion.

There is much disagreement with the above "classical" description and, since no reports could be found which compared the osseous changes of the two lesions in large series of pathologically proven cases, this study was accomplished.

The skull roentgenograms of 70 patients with chromophobic and 30 patients with eosinophilic adenomas were obtained from the Roentgen Department of Serafimerlasarettet and the Neuro-radiologic Department of Karolinska Sjukhuset, Stockholm, Sweden. All tumors were surgically treated and pathologically verified. For further comparison, the authors included 30 verified cases of craniopharyngiomas and 25 cases of optic gliomas. The normal sellar entrance was evaluated in 100 normal subjects.

Standard projections were utilized in evaluating sella, and its size was determined by the technique of Di Chiro *et al.* using the formula: $\frac{1}{2}$ length \times width \times depth. This was corrected for 70 cm. target skin distance and the maximum normal sellar volume was 1,220 mm.³ for these one-dimensional measurements. Degree of erosion was also noted and graded from +1 to +4. The results are summarized in 2 tables. Roentgenographic examples of each lesion are also included.

It was discovered that no individual feature of the "classical" description of the 2 main types of pituitary adenomas is pathognomonic of either type of tumor. In fact, not even 1 of the main "classical" changes described for 1 type of tumor may be accurate in the individual cases. Thus, an eosinophilic adenoma may have all of the features of a "classical" chromophobic adenoma and vice versa. In any large

series of patients, however, the balloon-shaped sella is predominantly found in eosinophilic adenomas, and the cup-shaped sella is found in chromophobic adenomas. In the differentiation between the lesions, most consistent was the lack of a minimal erosion of the dorsum sellae by the eosinophilic adenoma, and the similarity of the sellar entrances and volumes in both lesions.

It was found that the normal sella may have a cup-like or balloon-like appearance, but practically all the cases of pituitary tumors showed significant enlargement of the sella. In addition, optic gliomas and craniopharyngiomas could produce changes in the sella that could entirely mimic those of the adenomas. But this was unusual and changes produced by pressure from above the sella distinguished these lesions from the intrapituitary tumors. Calcifications, when present, were usually specific.

Finally, meningiomas, obstructive hydrocephalus with an enlarged 3rd ventricle, and generally increased intracranial pressure can cause sellar changes similar to those of the suprasellar and intrasellar lesions. In these cases, other osseous changes must be present to aid in the differentiation.—Paul M. Kroening, M.D.

EINSTEIN, ROBERT A. J. Sialography in the differential diagnosis of parotid masses. Surg., Gynec. & Obst., May, 1966, 122, 1079–1083. (From: Department of Therapeutic Radiology, Cedars-Sinai Medical Center, Los Angeles, Calif.)

The roentgenographic demonstration of the salivary ducts often furnishes information not available on physical examination. Incomplete or ambiguous clinical findings are not uncommon.

Sialography has been performed as an office procedure in a consecutive series of 357 patients during the past few years. The roentgenologic and surgical findings were correlated. Operation was performed in 265 patients, by the same surgeon. The remaining 92 patients were observed for a sufficient length of time to permit a satisfactory confirmation of the diagnosis.

Considerable anatomic variations in the size and shape of normal parotid glands and in the caliber and branching of the ductal system are noted. The intact ductal system resembles a winter tree, with evenly distributed branches gently tapering off toward the periphery. Stensen's duct normally measures not more than 3 mm. in diameter. The pathologic findings can be classified as: intrinsic space-occupying lesions; extrinsic indenting masses; and abnormalities of the ductal system.

Intrinsic space-occupying lesions are the most common finding, requiring anatomic localization. Well defined intrinsic space-occupying masses may produce rounded pressure defects in the major and lesser ducts. Deep lobe masses show a rather characteristic medial ballooning, which might be described as an umbrella effect. Masses compressing or displacing the distal part of Stensen's duct, such as tumors of the accessory lobes, are easily recognized. Frequently the mass cannot be clearly outlined; then, recourse must be taken to indirect evidence, such as ductal compression or displacement of a portion of the gland. Stereoscopy has been especially helpful in such instances.

Extrinsic masses often cause indentation or rotation and displacement of the entire gland. Distortions of this type are due to enlarged lymph nodes adjacent to the gland, tumors of the face and neck, or congenital anomalies.

Abnormalities of the ductal system are usually caused by inflammatory or neoplastic infiltrating processes. The findings include variations in the caliber of the entire ductal system, with irregular interruption of the continuity of the ducts, strictures, and sacculations, occurring especially in the terminal portions of the ducts.

The series included 218 neoplastic lesions. Of the 47 patients with nonneoplastic lesions, 11 presented advanced sialangiectasis.

The roentgenologic diagnosis proved correct in 256 or 96.6 per cent of the surgical patients and incorrect in 9. In 8 patients, the roentgenograms appeared to be normal, although there were small, clinically palpable masses—4 proved to be mixed tumors; 3, adenocarcinomas; and 1, an enlarged lymph node.

Diagnosis in the 92 patients treated clinically included: sialangiectasis, 33; sialadenitis, 3; hypertrophy of masseter, 14; angioma, 2; enlarged transverse process of the atlas, 1; Mikulicz's disease, treated by irradiation, 1; leukemia, 1; metastatic lymph node, 1; sebaceous cyst, 1; tuberculous adenitis, 1; and hypertrophy of gland, 1. In 26 instances, the mass disappeared spontaneously.

The roentgenogram was never topographically misleading.

Sialography is of particular value in the differentiation between surgical and nonsurgical diseases of the parotid gland and often prevents needless exploratory operations.

Preoperative pathologic differentiation of parotid tumors by roentgenography was not attempted, as it is not sufficiently reliable.—Stephen N. Tager, M.D.

Neck and Chest

Follis, G., and Marshall, T. R. The roentgen diagnosis of pulmonary histoplasmosis. *GP*, April, 1966, 33, 118–126. (From: University of Louisville School of Medicine, Louisville, Ky.)

The authors state that the value of roentgenography in pulmonary histoplasmosis has long been underrated. Certain roentgenographic patterns suggest this disease so strongly that the diagnosis should

be brought to mind merely by inspection of the chest roentgenograms.

The disease has a strong predilection for the Ohio, lower Missouri and Mississippi river valleys. No more than 5 per cent of infected persons appear to be seriously ill. Although whites and Negroes have an equal incidence of infection, symptomatic histoplasmosis occurs almost exclusively among whites. The most commonly observed lesions are pulmonary but the fungus can involve many parts of the body including the digestive system, the central nervous system, the bones, the larynx, the eye, the mediastinum and the mesenteric lymph nodes.

The most valuable of the laboratory aids is the histoplasmin skin test. The complement-fixation test is inconsistent. Biopsy is more reliable than culture.

There is lack of truly pathognomonic roentgen findings in pulmonary histoplasmosis. The acute pulmonary form may have a fine miliary or nodular distribution or it may be of the nondisseminated type with patchy, hazy or nodular infiltrates with or without hilar or mediastinal lymphadenopathy. The chronic pulmonary form may be of the fibrocavitary type with or without emphysema, or chronic lymphadenopathy may give rise to the middle lobe syndrome. In the healed type there may be small, miliary calcified pulmonary nodules, calcified lymph nodes, or larger single or multiple pulmonary nodules, with or without calcification. Broncholithiasis may be a sequel.

The treatment of histoplasmosis is difficult to evaluate. Amphotericin B is the drug of choice. Even with its use the prognosis in the fibrocavitary and disseminated type must be considered guarded, but without treatment the prognosis is poor.—Arthur E. Childe, M.D.

Pearson, F. G., and Thompson, D. W. Occult carcinoma of the bronchus. *Canad. M. A. J.*, April 16, 1966, 94, 825–833. (Address: Dr. F. G. Pearson, 904 Medical Arts Building, 170 St. George Street, Toronto 5, Ontario, Canada.)

The authors report 8 patients with "occult carcinoma" of the bronchus and compare their experience with 27 other patients described in two similar studies. In all these 8 patients routine chest roent-genograms failed to reveal the tumors. In 6 instances there had been an episode of pneumonia or hemoptysis, or both. The other 2 were investigated because of abnormal chest roentgenograms but in neither case was the obvious chest lesion the carcinoma.

Sputum cytology in this early type of carcinoma, unlike in more advanced cases, is very frequently positive, and it should be widely employed in the cancer susceptible group of patients—the smoking male over the age of 40 years. When positive, bronchoscopy should be carried out, including examina-

tion of bronchial secretions and bronchial washings. If the localization is still in doubt, bilateral bronchography is indicated. If there is still reasonable doubt of the locale of the lesion the same program should be repeated at 6 month intervals.

There is reason to believe that bronchial carcinoma in this in situ or early invasive stage is rarely multifocal but rather that it is a localized neoplasm amenable to curative therapy. None of these patients died from carcinoma during the post-treatment follow-up period which was continued for a minimum of 18 months.—Arthur E. Childe, M.D.

TIENE, E. SCHWARZ. Asthma in infancy. Minerva med., Jan.—Feb., 1966, 8, 1–6. (Address: Clinica Pediatrica dell'Università, Milano, Italy.)

Bronchial asthma in adults and children refers to a respiratory disease characterized by more or less severe and prolonged attacks of expiratory dyspnea, mucosal edema accompanied by spasm of the bronchial smooth musculature and increased mucus secretions. These attacks result in permanent anatomic changes of the thorax and respiratory system involving emphysema, bronchiectasis, etc.

In a large percentage of cases of asthma in the adult, the disease dates back to early years of life and has become chronic, as a rule, through an inadequate assessment of its importance and the likelihood of its running an unfavorable course. The author states that there is a need that attention of physicians be drawn to this respiratory disease of childhood which, when and if suitably treated, carries a more favorable prognosis than asthma of adolescence or adulthood.

The disease, arising in the early years of life, is marked by increasingly frequent and severe attacks. There is a wide variety of respiratory symptoms: in children, mucus hypersecretion predominates over bronchial spasms giving a picture of asthma-like subacute tracheobronchitis, an important pathogenic role being assumed by infective factors.

The roentgenographic findings, as shown by the author, are increased in the bronchial markings caused by a peribronchitic density around the bronchial branches; there may also be some evidence indicating pulmonary emphysema.

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The author gives a fairly comprehensive discussion of the etiology and the symptomatology as well as treatment of the condition.—C. Peter Truog, M.D.

Webster, J. R., Jr., Saadeh, G. B., Eggum, P. R., and Suker, J. R. Wheezing due to pulmonary embolism: treatment with heparin. New England J. Med., April 28, 1966, 274, 931-933. (From: Departments of Medicine, Northwestern University Medical School and Chicago Wesley Memorial Hospital, Chicago, Ill.)

The purpose of the authors is to call attention to the occurrence of wheezing due to pulmonary embolism—a physical finding that is probably more common than is generally appreciated, and to discuss the place of heparin in its treatment. They report 3 cases with acute onset of wheezing, pain in the chest and dyspnea with wheezing being the presenting symptom of pulmonary embolism.

The mechanism of the bronchoconstriction that these patients demonstrated was most probably the release of serotonin from circulating blood platelets, which were either attracted to or attached to the thrombus. It is of practical therapeutic importance that this release can be prevented by heparin administration, although heparin apparently has no pharmacologic effect on histamine or serotonin released before its administration. This blocking action may prove to be of critical importance in the management of acute pulmonary embolism.

Of the 3 patients reported only I showed any evidence of pulmonary pathology in the chest roentgenogram. Radioisotope lung scans, however, revealed evidence of the pathology.

The authors conclude that appreciation of the occurrence of bronchoconstriction and wheezing in pulmonary embolism should allow earlier and more frequent recognition and hence more satisfactory management of pulmonary embolic disease. They also conclude that the use of heparin appears to be of special therapeutic value once the diagnosis has been made.—C. Peter Truog, M. D.

ABDOMEN

RUSSELL, WARREN M., and MARGULIS, ALEXANDER R. Thickness of the gastric wall determined by megavoltage roentgenography. Radiology, April, 1966, 86, 707-710. (Address: Department of Radiology, University of California, San Francisco Medical Center, San Francisco, Calif.)

Diagnostic roentgenograms obtained with the use of generators of 1,000 or higher kvp. have potential advantages over conventional roentgenograms. The similar absorption coefficients at this energy level for soft tissue and bone and a wide separation of these coefficients and that of air, or other gas, enhance the visualization of structures outlined by a gas. Therefore, an experiment was designed to determine whether, in examining the air-outlined gastric wall, megavoltage roentgenograms offered advantages over conventional roentgenographic examinations.

One or more artificial tumors were implanted into the gastric wall of 24 New Zealand white rabbits and 10 mongrel cats. The stomachs of these animals were filled with air, an artificial pneumoperitoneum was done, and "plain films," tomograms, and megavoltage roentgenograms were obtained. Following this initial evaluation, 2 patients were examined by the 3 roentgen procedures. In the rabbits, the "plain" and megavoltage studies yielded essentially the same results and the tomograms yielded a higher incidence of "false tumor." Collectively, the 3 procedures yielded a 90 per cent accuracy. Tumor of the lesser curvature and antrum was more often incorrectly diagnosed. In the cats, tomograms and megavoltage study yielded equal and slightly better than 90 per cent accuracy but only 80 per cent accuracy by "plain film" evaluation. Together, the 3 procedures gave a 100 per cent result and no incidence of false positives. Surgical evaluation of 2 patients with suspected stomach lesions, examined by the 3 roentgen procedures, confirmed the presence of a lesion in each case.

The results of this study indicate that megavoltage roentgenograms would appear to nearly equal the accuracy of tomography. The exposure dose is less and, in most instances, the time required for the examination is probably considerably shorter. However, additional evaluation of this technique is indicated.—John L. Bond, M.D.

DAVES, MARVIN L. Clatworthy's sign. Radiology, March, 1966, 86, 480-481. (Address: University of Colorado Medical Center, Denver, Colo.)

This article deals with the roentgenographic significance of anterior displacement of the duodenum in the pediatric patient with portal hypertension.

Anterior displacement of the duodenum in children with extrahepatic portal hypertension was first described by Clatworthy and Boles in 1959. They reported II cases with portal hypertension and 4 of these cases were infants with roentgenologically demonstrable anterior displacement of the duodenum which, at surgery, revealed extensive retroperitoneal fibrosis and edema. Their conclusions were: (1) retroperitoneal fibrosis and edema should be considered in the differential diagnosis of pediatric portal hypertension; (b) the presence of anterior duodenal displacement should suggest restraint to operative intervention; and (c) improvement of the patient is likely to occur with lapse of time, at which time the duodenum will have returned to normal position and the operability of the patient will have improved.

The author reports a single case, a 6 year old white female, with portal hypertension, suspected because of esophageal varices, splenomegaly, and demonstrable anterior displacement of the duodenum. Splenoportogram showed a thread-like obstructed splenic vein. Laparotomy failed to reveal an adequate portal vein within the extensive fibrosis and edema, preventing a shunting procedure.

Clatworthy's sign is anterior displacement of the duodenum, produced by retroperitoneal edema, in a patient with portal hypertension. A positive Clat-

worthy's sign is a contraindication to surgical intervention.—John Bond, M.D.

Patterson, Marcel, Ong, Helen, and Drake, Arnold. Protein-losing enteropathy: report of two new cases. Am. J. M. Sc., May, 1966, 251, 563-569. (From: Department of Internal Medicine, University of Texas Medical Branch, Galveston, Texas.)

The numerous gastrointestinal diseases associated with hypoproteinemia are listed. Patients with idiopathic hypoproteinemia and with small intestinal abnormalities are seen who do not fall into any known clinical entity. The case reports of 2 patients in the latter category are given. Both had roentgenologically abnormal small intestinal studies, but with entirely different clinical pictures.

Although all the causes of protein loss from the small intestine are not defined, lymphatic obstruction seems proven. The congenital form is thought to possibly be a variant of Milroy's disease. Retroperitoneal fibrosis, neoplasm, or granulomatous disease may be the cause of the acquired form of intestinal lymphatic obstruction. Denuded mucosa, as seen in regional enteritis and diffuse ulcerative disease, is also a well-recognized cause of protein loss from the small intestine. In other patients, the pathogenesis is obscure.—Mark D. Reiss, M.D.

Kune, G. A. Megacolon in adults. *Brit. J. Surg.*, March, 1966, 53, 199–205. (Address: Royal Melbourne Hospital, Melbourne, Australia.)

Twelve adults with megacolon have been divided into 3 groups according to the site of involvement. It has been found that each group behaves in a different manner on physiologic investigation and requires a different form of treatment. All patients had rectal biopsies which demonstrated autonomic ganglion cells, thus excluding Hirschsprung's disease.

Barium enema study showed dilatation of the entire colon and rectum with megacolon and megarectum in 7 patients of Group 1. The patients complained of constipation with defection occurring every 3–12 days. Anal sphincter tone was normal and sigmoidoscopy showed no abnormality. These patients were best managed conservatively.

Two patients of Group 2 presented with recurrent episodes of abdominal pain and distention and absolute obstipation. Roentgenographic examination and subsequent surgical exploration disclosed marked dilatation of the sigmoid or megasigmoid, while the proximal colon and rectum were normal. The possibility of recurrent volvulus was suggested. Excellent therapeutic results were obtained by sigmoid resection and anastomosis with the normal rectum.

Group 3 consisted of 3 elderly female patients with megasigmoid and megarectum, who presented with symptoms of subacute large bowel obstruction. No obstructing lesion was shown by the barium enema study and the proximal colon appeared normal. The anal sphincter was tight and the rectum was markedly dilated and unresponsive to dilatation. Such patients may respond to conservative management by rectal tube drainage, but have required sigmoid resection and colostomy.—David Corbett, M.D.

KAYE, JOSSE, SOLOMON, A., and LAZAR, S. J. Further experience with Dulcolax in barium enema examinations. *Med. Proc.*, March, 1966, 12, 111–117. (From: University of the Witwatersrand, Johannesburg, and Department of Radiology, Johannesburg General Hospital, Johannesburg, South Africa.)

The authors report on the use of Dulcolax in propylene glycol in 519 recent barium enema examinations. The use of this contact evacuant in the enema fluid improved the evacuation of barium and thereby provided a better study of the mucosal pattern of the colon. No toxicity was reported with the use of this agent.

Selected cases are included to emphasize the value of good mucosal studies.—John D. Shoop, M.D.

Boyd, Eldon M., and Abel, Miriam. The acute toxicity of barium sulfate administered intragastrically. *Canad. M. A. J.*, April 16, 1966, 94, 849–853. (From: Department of Pharmacology, Queen's University, Kingston, Ontario, Canada.)

As part of a basic research project designed to estimate the toxicity of tannic acid-barium sulfate enemas used in diagnostic radiology, a separate study was undertaken to determine the toxic effects of barium sulfate by itself. A 150 per cent solution of barium sulfate was introduced into the gastric cavity of male albino rats through an intragastric cannula in total doses of 188, 225, 263, 300, 338, and 375 gm./kg. Fifty rats were kept as controls and were given distilled water through the intragastric cannula to a maximum dose of 185 ml./kg.

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Of the animals given the barium sulfate solution, it was found that 50 ultimately died of stomach rupture, the LD₅₀ being 307 ± 29 gm./kg. This occurred most commonly along the lesser curvature. It was associated with arteriovenous thromboses in many of the other organs of the body. The cause of death therefore was stomach rupture due in part probably to pylorospasm, followed by extensive arteriovenous thrombosis which produced hypothermic respiratory failure. Death in those animals which survived stomach rupture was due almost exclusively to bowel obstruction, the LD₅₀ being 364 ± 41 gm./kg. The immediate cause of death was respiratory failure preceded by convulsions or cyanosis. At autopsy an im-

paction was always found in the small bowel and usually in the colon as well, with associated arteriovenous thromboses. These were even more widespread than in the group that died of stomach rupture and could be found in all organs of the body.

Of those animals that survived these large doses of barium sulfate, most were clinically well within 72 hours of the initial administration. Most of the deaths occurred from doses that were between 25 per cent to 40 per cent of the calculated body weight. When the results of this study were extrapolated to man, it was found that barium sulfate could probably not be taken by mouth in single doses sufficiently great enough to produce signs of toxicity.

The authors conclude that barium sulfate does not appear to be a factor of significance in the acute toxicity of tannic acid-barium sulfate solutions used in diagnostic radiology.—Kenneth M. Nowicki, M.D.

GYNECOLOGY AND OBSTETRICS

MILNE, E. N. C. Orthodiagraphic shift pelvimetry. J. Canad. A. Radiologists, March, 1966, 17, 29-37. (From: Victoria Hospital, London, Ontario, Canada.)

The orthodiagraphic principle implies that the image of the object being radiographed should be an exact representation of the object itself, without magnification. The further the roentgen-ray tube is from the object, the more parallel its rays will be. Thus, using a very large anode-to-film distance is one method of obtaining a relatively orthodiagraphic projection. An alternative to this is to center the tube on the margins of the object to be radiographed—and expose one film with a collimated beam, and then to displace the tube to the other margin of the object and repeat the exposure. This ensures that the margins of the object are orthodiagraphically projected and the total width of the object is thereby accurately represented.

The patient lies supine, exactly in the midline of the roentgenographic table. The tube is tilted 15 degrees towards the feet and centered to the midline at the level of the anterior superior iliac spines. The beam is collimated to a narrow vertical band, 2 cm. to 4 cm. wide and 12 cm. long, and the tube is displaced 5 cm. to one side of the center and an exposure made. The tube is then displaced 5 cm. to the opposite side of the midline and a second exposure made. The lateral roentgenogram is made with the patient erect. No opaque rule is employed. Instead, the distance from the natal cleft to the film is measured and the anode-to-film distance set at five times this measurement, ensuring a known constant magnification of 25 per cent. This is facilitated by using a ruler graduated in fifths of an inch. The anode-to-film distance in inches then equals the number of divisions recorded on the ruler.

Many present-day methods of pelvimetry suffer from complexity, inaccuracy and excessive irradiation. The orthodiagraphic shift technique, as described in this paper, has been shown to be accurate and to give a much reduced radiation dose. Measurements of the pelvis are taken directly from the film, using a transparent ruler. This ruler bears a logarithmic scale from which pelvic areas can be immediately assessed by addition and subtraction only.—Eugene J. McDonald, M.D.

FERRIS, ERNEST J., SHAPIRO, JEROME H., and SPIRA, JACOB. Roentgenologic aspects of intrauterine transfusion. J.A.M.A., May 16, 1966, 196, 635-636. (Address: Dr. Ferris, 818 Harrison Avenue, Boston, Mass.)

This is a follow-up study from Boston City Hospital of the technique and results of 50 intrauterine transfusions in 24 women for erythroblastosis fetalis.

Under sedation and closed circuit image intensification television at 100 to 110 kvp. and 1.5 to 3.0 ma. a site of fetal puncture below the rib cage is selected. A small amount of meglumine diatrizoate is injected to verify needle-tip position and when checked, packed red blood cells are injected.

Phantom studies show an exposure of 280 millirads to the fetus.

The authors do not minimize the risk and mention a lacerated myocardium, peritonitis, a retained catheter tip and massive uterine hemorrhage as complications.

Because of the poor prognosis if the disease is left unattended, this procedure is gaining momentum. Cooperation of obstetrician and radiologist is urged with the use of image intensification and television monitoring.—Eugene J. McDonald, M.D.

Queenan, John T., Anderson, Gerald G., and Mead, Philip B. Intrauterine transfusion by the multiple-needle technique. J.A.M.A., May 16, 1966, 196, 664-665. (Address: Dr. Queenan, I Perryridge Road, Greenwich, Conn.)

The authors quote Liley's first successful transfusion and present their own last 12 intrauterine transfusions in fetuses under 28 weeks' gestation.

Two needles are used: the first to stabilize the fetus and serve as a guide to the insertion of the second needle.

Palpating to locate the fetal buttock the operator inserts the *first* needle or guide (20 gauge, 6 inch) into the amniotic cavity and 10.0 cc. hypaque M-75 is injected. The contrast medium may demonstrate soft tissue edema, indicating a poor prognosis. The needle is then advanced until the operator can feel it meet resistance of the fetal soft tissue. One half cc. of contrast medium is injected and an anteroposterior roentgenogram is made, confirming the position.

The second or "transfusion" needle is then placed through the fetal abdominal wall below the liver and spleen and 3 cc. of contrast medium injected to confirm the position in the fetal peritoneal cavity. The appropriate amount of packed red blood cells is then given. The average number of roentgenograms per transfusion procedure was 3. The fetal dosage is not given nor is the fetal salvage mentioned.—Eugene J. McDonald, M.D.

TALLEDO, E., CARTER, W. F., BRUNS, W. L., and ZUSPAN, F. P. Opacification of the amniotic fluid for localization of the placenta. South. M. J., May, 1966, 59, 581-584. (From: Department of Obstetrics & Gynecology, The Medical College of Georgia, Augusta, Ga.)

Amniocentesis is performed and hypaque 75 per cent (30 to 50 ml.) is injected into the amniotic fluid. A lateral roentgenogram centered at the iliac crest is usually all that is required. Corroboration of the diagnosis was made at cesarean section, by manual removal of the placenta or by distention of the amniotic sac.

Amniography was performed in 32 patients. In 19 it was for the sole purpose of placental localization, in 8 for diagnosis of fetal life, in 2 for multiple pregnancy, in 2 for Rh incompatibility, and in 1 for polyhydramnios. Regardless of the indication, the placental site was diagnosed in 31 out of 32 patients. The 1 failure was encountered in the patient with polyhydramnios and was thought to be due to insufficient amount of contrast medium.

Premature labor was not encountered in viable pregnancies. Delivery occurred in 6 of 8 patients with fetal death *in utero*.

In pregnancies under 32 weeks, studies of the soft tissue for placental localization are not very accurate. Amniography on the other hand does not have this disadvantage, since it localizes the placenta directly by increasing the density of the amniotic fluid, thereby accentuating the filling defect created by the placenta on the contour of the amniotic sac. In conditions known to impair the visualization of the placenta by conventional techniques, such as obesity, polyhydramnios, multiple pregnancy, breech presentations, and presence of intestinal gas or fecal material in the colon, amniography will give more reliable results.—Eugene J. McDonald, M.D.

COOPER, R. D., Jr., IZENSTARK, J. L., and WEENS, H. S. Placental scanning with iodine-131. J. Nuclear Med., April, 1966, 7, 304-307. (From: Division of Nuclear Medicine, Department of Radiology, Emory University School of Medicine and Grady Memorial Hospital, Atlanta, Ga.)

Point count localization and rectilinear scanning are the alternative radioisotope methods of placental localization. The former technique requires repeated repositioning of the probe, and thus is somewhat laborious to perform. Various groups have found it to be rather accurate however. Localization of the placenta by scanning was made more popular, as well as more rapid and certain, by the development of Tc^{99m} labeled human serum albumin as a tracer by McAfee *et al.* This tracer substance is not freely available, however, and is difficult to prepare in a sterile, injectable and pyrogen-free form.

The authors make a case for scanning with I^{131} labeled HSA in small doses of $5 \mu c$. A combination of moderate scanning speeds and wide spacing of scan lines allows them to scan the region of interest in about 20 minutes. In an experience of about 100 placental scans, localization accuracy appeared to be as good as that obtained with multiple point counting.

The authors feel that scanning is superior in that it is easier to perform with readily available tracers and commercial instruments.—Frederick J. Bonte, M.D.

GENITOURINARY SYSTEM

BLOOMFIELD, J. A. (Hobart, Tasmania.) Infusion pyelography in renal insufficiency. *Australasian Radiol.*, Feb., 1966, 10, 49–54.

Drip infusion pyelography, as described by Schencker in 1964, was used to study 23 patients with clinical evidence of renal insufficiency. The majority of the cases had blood urea nitrogen levels greater than 100 mg. per cent, and with the highest being 400 mg. per cent. A dose of 1 ml./lb. body weight of a contrast agent, such as 60 per cent hypaque, in an equal amount of 5 per cent dextrose solution, was given intravenously in about 10 minutes. Roentgenograms were taken at the end of the infusion and then as needed to demonstrate the pathology.

Roentgenologic appearances in cases of renal insufficiency fell into 2 main groups. One group consisted of patients with extensive nephron failure (diffuse glomerulo-nephritis) in whom the resulting nephrograms were poor and the faintly defined pyelograms were relatively normal. The patients in the second group had obstructive lesions, such as pelviureteric block, and had some functioning renal tissue that permitted visualization of the surviving renal cortex and eventually the obstructed portion of the renal tract.

Opacification of the normal tissue permits the outlining of renal cysts and similar avascular lesions. The crescent sign of Dunbar was described and occurs when the opaque medium is concentrated in the surviving renal cortex. It may be seen in cases of hydronephrosis, polycystic disease or chronic pyelonephritis. The crescent sign occurs early in the study and is usually seen in the initial nephrograms. There may be a delay of several hours before the calyces and pelvis are demonstrated in cases of obstruction.

Opaque media are preferentially excreted by either the liver or kidneys depending on the protein binding capacity. The liver appears to clear the media from the blood when the kidneys are unable to do so.

Drip infusion pyelography is a supplemental and not a routine procedure and has proved to be a valuable technique in the investigation of renal insufficiency even in the presence of high blood urea. The high doses of contrast media apparently have no adverse effects. The technique has helped to differentiate surgical from nonsurgical lesions.—*Charles W. Cooley, M.D.*

Voltz, Phillip W., Jr., Thaggard, Alvin, Jr., O'Neill, Francis Edw., Wiesner, Jerome J., and Douglass, Clifton F., Jr. Large dose urography in children. South. M. J., May, 1966, 59, 519–524. (From: Santa Rosa Medical Center, San Antonio, Tex.)

This report is an evaluation of the routine use of large doses of contrast material for urography in children at the Children's Hospital of Santa Rosa Medical Center, San Antonio.

The authors used sodium and methyl glucamine diatrizoate (Renovist). The dosage schedule was: Newborn to 10 pounds, 10 cc.; 10 pounds to 2 years of age, 10–25 cc. (no more than 1 cc. per pound); 2 years of age and older, 25 cc.; and 100 pounds or 14 years of age, 50 cc.

Two hundred examinations were selected for evaluation. Eighty per cent were considered excellent or comparable to the detail obtained from a good retrograde study. Two were unsatisfactory due to technical factors, such as extravasation of contrast medium. Three poor but diagnostic studies were obtained in patients with azotemia, in which the blood urea nitrogen ranged from 51 to 66 mg. per 100 ml. Unsatisfactory studies were also obtained in the neonatal period, either due to the limited glomerular filtration in this age group or the opacification of other organs and viscera with the large dose of contrast material.

The increase in dose is considered by the authors as the greatest single factor in improving the excretory urogram.—David Corbett, M.D.

Garusi, G. F. Valutazione critica sulla importanza della indagine radiologica nello studio dell'ipertensione reno-vascolare. (A critical assessment of the importance of radiology in the investigation of renal vascular hypertension.) *Minerva med.*, Sept., 1965, 56, 3011–3030. (From: Istituto di Radiologia dell'Università di Bologna, Bologna, Italy.)

The study of renal vascular hypertension initiated by the classic experiments of Goldblatt in 1934 has

had an impetus because of the favorable results obtained by modern vascular surgical techniques.

The author presents an exhaustive study of 12 patients affected by renal vascular hypertension and a comparison with the results of other investigators.

A synopsis of the radiologic criteria includes direct and indirect findings.

- A. Direct—Visualization of the stenosis by angiography.
- B. Indirect—Post-stenotic dilatation, greater intensity and prolongation of the nephrographic phase, presence of collateral circulation, diminution of renal volume.

The methods and signs determining these criteria are:

- (1) Excretion urography by serial exposures at short intervals which is a useful preliminary study.
- (2) Unilateral renal ischemia, reduction in the dimensions of the renal shadow, retarded and decreased visualization of the renal collecting system on the affected side, and at times delayed hyperconcentration of the opaque medium.
- (3) Small marginal defects of the renal pelvis and uppermost portion of the ureter representing collateral circulation caused by stenosis of the renal artery.
- (4) Renal aorto-arteriography, which is undoubtedly the most valuable method for demonstrating obstructive arteriopathy in its various phases, arteriographic, nephrographic and eventually urographic; it not only depicts the morphologic aspects of the arteriopathy, *i.e.*, site, type, extent of the stenosis, but also the hemodynamic aspects, *i.e.*, time of appearance and duration of the nephrogram, dimension and intensity of the renal shadows, presence of collateral circulation.
- (5) Aorto-arteriography will also demonstrate other vascular malformations such as aneurysms, and arterio-venous fistulae which likewise produce hypertension.
- (6) In comparison with selective renal arteriography, aorto-arteriography is advantageous because of simultaneous visualization of the aorta and of both renal vascular systems. Selective renal arteriography will facilitate diagnosis of localized lesions of a lesser extent and in a segmental or accessory branch.
- (7) The significance of the angiographic criteria is not constant or certain in all cases. The investigation is to be carried out with a prior proper selection of the patient, and the results evaluated with caution. One must not forget that obstructive renal arteriopathy in certain hypertensive patients may not be the primary cause but a concomitant manifestation of a more generalized process; that in some instances it is not possible to correlate the type of the stenosis and the severity of the renal ischemia and the resulting functional and morphologic alterations; that renal artery stenosis, especially of the atheromatous

type, may exist in patients with hypertension of different etiology and even in normotensives.

It is evident that the diagnosis in the light of an eventual surgical intervention should be based on a careful and complete clinical investigation.—Anthony A. Blasi, M.D.

Erman, H., Jacobsson, B., Kock, N. G., and Sundin, T. High diuresis, a factor in preventing vesicoureteral reflux. J. Urol., April, 1966, 95, 511-515. (From: Surgical and Roentgendiagnostic Departments, Sahlgrenska Sjukhuset, University of Göteborg, Sweden.)

Twenty-nine adult patients, in whom vesicoureteral reflux had been previously demonstrated during micturition, were investigated in this study as regards the effect of urinary output upon intermittent vesicoureteral reflux.

The first 5 patients were examined by the isotope method using radioactive gold by bladder infusion. By this method, it is possible to demonstrate reflux into the renal pelvis but minimal reflux into the lower ureters could not be detected because of the masking effect of radiation from the isotope in the bladder. The remaining 24 patients were studied radiographically by continuous television fluoroscopy and cineradiography. The equipment allowed examination of patients only in the supine position and many people cannot void in such a position. For this reason, most of the patients studied have low pressure reflux. In all 29 patients, the intravesical pressure was continuously recorded through a special urethral catheter.

The patients were first examined after fluid intake had been restricted for at least 12 hours. Five hundred cc. of 15 per cent mannitol solution was infused intravenously in 20–30 minutes and the radiographic examination of the bladder and lower urinary tract was repeated. The diuresis during the investigation was calculated as the difference between the volume of the bladder contents at the end of the examination and the volume infused into the bladder.

Of the 5 patients studied by the isotope method, all had reflux to the renal pelvis on the dehydration examination. After the mannitol infusion, no reflux was recorded in 2 cases and in 2 other cases the reflux appeared later and at a higher pressure. In I case the reflux was unchanged.

Of the 24 patients who exhibited vesicoureteral reflux during dehydration, reflux was completely inhibited by the mannitol infusion in 3 patients, and in 4 patients total reflux was turned into partial reflux since it extended to the lower ureter only. In 4 patients, reflux appeared at a larger bladder volume and at a higher bladder pressure than during the dehydration study. In 13 patients, the reflux was not influenced by increased diuresis. Eleven patients were unable to void in the supine position either on the dehydration study or on the hydration portion of

the examination. In the 3 patients in whom reflux disappeared completely, micturition roentgenograms were obtained.

A study of the urinary output showed an average of 0.7 cc. per minute from both kidneys before mannitol infusion and 9.3 cc. per minute after mannitol infusion.

The authors discuss the various possible mechanisms by which ureteral reflux is diminished or abolished by high diuresis. It is possible that low pressure reflux is more significantly influenced by high diuresis than high pressure reflux. This is of particular importance since low pressure reflux is more likely to cause renal damage and this is the type of reflux which is most likely to occur in children. Low pressure reflux or continuous reflux is present in some patients during most of the day or night while high pressure or momentary reflux acts only during micturition.

From this study, it is evident that all patients undergoing investigation for vesicoureteral reflux should be on fluid restriction for the previous 12 hours. This is important both for the initial diagnosis and for the subsequent comparative studies. High fluid intake should be added to the other routine procedures for the conservative treatment of vesicoureteral reflux. The highest possible diuresis which does not interfere with the patient's nightly rest is the recommended therapy.—George W. Chamberlin, M.D.

Melick, W. F., Brodeur, A. E., Herbig, F., and Naryka, J. J. Use of a ureteral pacemaker in the treatment of ureteral reflux. J. Urol., Feb., 1966, 95, 184–196. (Address: Dr. Melick, 3720 Washington Avenue, St. Louis, Mo.)

Experimental work using hydronephrotic pig ureters disclosed that it is possible to stimulate them anywhere along the course of the ureter and that prolonged electrical stimulation with currents up to 12 volts did not produce any untoward complications, either locally or on the cardiovascular system of the animal. In a previous study, it was found possible to reverse a segment of pig ureter and have it work normally. This experiment indicated that there was little or no extrinsic nerve innervation involved in ureteral peristalsis.

The authors report 4 patients who have had advanced low pressure vesical ureteral reflux. The first, a 7-month-old boy illustrates the fact that simple cutaneous vesicostomy will, over a relatively long period of time, allow the ureteral muscle to return to normal or near normal. Two other children showed some improvement after a Y-plasty operation and cutaneous vesicostomy, but the ureteral pressures did not return to normal and the reflux was not eliminated. In these 2 patients, added improvement was obtained by implanting a ureteral pacemaker with the ground wire attached to the capsule of the

kidney and the other electrode to the proximal ureter. After some months of stimulation, ureteral pressures and ureteral peristalsis returned to normal and little or no vesical ureteral reflux was subsequently demonstrated. In the fourth patient, an II-year-old child with massive bilateral vesical ureteral renal reflux, the parents refused to consider any form of urinary diversion. A pacemaker attached to the right urinary tract produced some temporary improvement after 2 months of stimulation, and the unpaced left ureter showed no change. When stimulation was discontinued, the right ureteral pressures returned to a low level and peristalsis was completely lost.

These studies indicate the need for urinary diversion in cases of severe vesical ureteral reflux and in certain instances the use of electronic pacemakers to restore normal ureteral muscle tone.—George W. Chamberlin, M.D.

GARDINER, J. H. Radiologic observations associated with phenacetin overdosage. J. Canad. A. Radiologists, March, 1966, 17, 21–28. (From: Toronto Western Hospital, Toronto, Ontario, Canada.)

The changes in 8 cases (7 women and I man) of kidney damage associated with phenacetin overdosage have been studied in detail.

The evidence incriminating phenacetin ingestion as a cause of renal disease is highly circumstantial. Most investigators feel that prolonged excessive use of mixed analgesic compounds containing salicylate and phenacetin can lead to kidney damage. The microscopic changes in the kidneys of a patient who has abused phenacetin are not really different from those of pyelonephritis. The papillary necrosis frequently observed in this condition does not appear to be different from that found in case of diabetes or urinary tract obstruction.

Interstitial nephritis is frequently encountered in pathologic specimens from these cases. All stages of pyelonephritis are found. A high incidence of papillary necrosis in the more advanced cases is striking.

There are two types of necrosis, a papillary form and a medullary form, according to which portion of the pyramid becomes necrotized. Either or both types may be found in either or both kidneys at the same or different times.

The kidneys are usually normal in size. If the renal outlines are smaller than normal, it is due to chronic inflammation and frequent association with pyelonephritis.

Renal function may be so impaired by the time the patient is seen that satisfactory visualization of the collecting systems is not possible by intravenous pyelography. Six of the 8 patients reported initially had unsatisfactory pyelograms. Reduction in function may be localized, with loss of definition and blurring of one or a few calyces. With progression of

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the disease process, subsequent pyelograms may demonstrate changes of papillary necrosis in areas where earlier there had been simply impaired function.

The pathologic changes are usually bilateral.

Roentgen findings. The roentgenographic appearances may be indistinguishable from those of pyelonephritis, with calyceal blunting and club-shaped deformities.

Necrotic papillae. The characteristic roentgenologic appearance of papillary necrosis is the so-called "ring sign." The ring is observed when contrast medium surrounds a necrotic papilla within a cavity. In the medullary type of necrosis the ring is usually round or oval. With papillary necrosis, the ring is more often triangular in shape.

Peptic ulceration. Many patients ingesting excessive quantities of analgesics give a history of gastric or duodenal ulceration. Six of the 8 cases in this study had a history of ulcer; 3 of them required surgery for ulceration prior to the development of the urinary tract symptoms.

Differential diagnosis. Before cavities have formed, blunting, widening and irregularity of the calyceal fornices may simulate pyelonephritis or renal tuberculosis. When a cavity forms, other conditions which are also associated with production of cavities need to be differentiated. These include tuberculosis, diverticulum, cyst and sponge kidney.

It is important that the radiologist recognize the roentgen changes and be prepared to suggest the possibility of analgesic nephritis together with the other causes of necrotizing papillitis and similar renal abnormalities.—Stephen N. Tager, M.D.

László, F. A., Kovács, K., Dávid, M. A., Sövényi, E., and Kocsis, J. Angio-renographic studies in oestrone-pretreated adrenalectomized and hypophysectomized rats following administration of posterior pituitary extract. *Med. Pharmacol. exp.*, 1966, 14, 70–77. (From: Department of Medicine and Department of Radiology, University Medical School, Szeged, Hungary.)

Through the use of angiocardiography supplemented by periodic histologic examinations, the authors studied the effect of exogenous posterior pituitary extract on the kidneys of estrogen pretreated rats. The experiment was performed utilizing female albino rats who had been given subcutaneous injections of estrone over a 10 day period. One group had recently undergone hypophysectomy, while another group had had prior adrenalectomy. A third group consisted of intact animals. All received variable amounts of posterior pituitary extract subcutaneously.

The authors discovered that the intact animals developed an acute tubular necrosis after injection of the posterior pituitary extract. This was found to be due to prolonged renal vascular spasm causing cellu-

lar hypoxia and ultimately tubular necrosis. Similar alterations were found in the adrenalectomized group. The third group of rats, consisting of those who had had previous removal of the pituitary gland, failed to exhibit significant renal disease. Although renal vascular spasm was noted to occur initially in this group, as in all the others, the authors theorized that tubular necrosis did not develop because the oxygen requirement of the kidneys became markedly less and thus the tubular cells were better able to tolerate the hypoxic state. Since tubular necrosis did occur in the absence of adrenal tissue, it was surmised that the decrease in adrenal cortical secretions usually seen in the absense of pituitary stimulation does not play a decisive role in the prevention of renal lesions.—Kenneth M. Nowicki, M.D.

RADIATION THERAPY

RESZEL, PAUL A., SOULE, EDWARD H., and COVENTRY, MARK B. Liposarcoma of the extremities and limb girdles: a study of two hundred twenty-two cases. J. Bone & Joint Surg., March, 1966, 48-A, 229-244. (From: Sections of Surgical Pathology and Orthopedic Surgery, Mayo Clinic and Mayo Foundation, Rochester, Minn.)

The authors present an extensive clinico-pathologic review of 222 cases of liposarcoma of the extremities and limb girdles from the files of the Mayo Clinic. Liposarcoma represents approximately 16 per cent of soft tissue sarcomata, exclusive of those in the retroperitoneum.

Liposarcoma may be defined as a malignant tumor of lipoblasts. A classification based on gross and microscopic appearance was made to include the following 3 pathologic types: myxoid, lipogenic, and pleomorphic. In turn, these 3 types were graded 1 through 4, according to the degree of differentiation of the malignant lipoblasts. On this basis myxoid tumors constituted 46 per cent of the group, lipogenic tumors 20 per cent, and pleomorphic tumors 33 per cent.

No associated clinical factors such as obesity, coexistent but independent lipoma, or trauma at the site of tumor formation were revealed. The mean age of the patients was 50.2 years at the time of initial diagnosis. The age range was 9 years to 81 years. There was a male to female ratio of 1.6 to 1, which is in contrast to the preponderance of lipomata in females. The lower extremity was the site of tumor three times more often than the upper and the proximal portions of the limbs were affected more often than the distal. The thigh was the site of tumor in 55.4 per cent of the cases.

The roentgenograms of 66 of the patients with liposarcoma were reviewed. The tumor appeared to be predominantly more radiopaque than the adjacent muscle in 28 and less opaque in 11. Ten of these 39 tumors had areas of both increased and decreased

radiodensity. No tumors were visible on 27 roent-genograms. Flecks of calcium were noted in 7 of the 66 tumors. The roentgenographic appearance seemed to depend on the type of tissue being produced; those producing minimum amounts of adult fat were not radiolucent.

Metastases were demonstrated in 45 per cent of the 166 patients followed 5 years or more after initial treatment. The average time of development of the metastases was 3 years and 8 months. The most common site of metastases was the lung. The size did not correlate with the tendency to metastasize. The grade or degree of malignancy was the most significant feature related to the tendency to metastasize.

Of 166 patients available for analysis 5 years after treatment, 55 per cent were dead. Of 52 patients followed 10 years or more after treatment, 9 had died of tumor and 6 had died of other causes, leaving 22 per cent who lived 10 years or more.

A review of the literature, numerous tables, and several photographs, photomicrographs, and roent-genographic reproductions are included in this excellent article.—Donald S. Linton, Jr., M.D.

Hughes, J. Howell, and Patel, A. R. Swelling of the arm following radical mastectomy. Brit. J. Surg., Jan., 1966, 53, 4–15. (From: The Royal Infirmary, Liverpool, England.)

Nineteen women with swollen arms after radical mastectomy were studied as to etiology and 15 had exploration.

Lymphangiography showed obstruction to lymphatic flow in the axilla and the main lymphatic trunks were tortuous. The dermal lymphatics had a diffuse reticular pattern. Phlebography demonstrated various degrees of venous obstruction without adequate collateral circulation. The axillary vein showed deformity with irregular filling and constriction; the valves were absent.

At surgery, in the absence of recurrent malignancy, the cause of the obstruction was found to be fibrosis. This compressed the axillary vein and there was a constricting sheath around the vessel and involving its wall. The cephalic vein also was involved in the majority of cases.

All 12 patients who had decompression of the axillary vein and any remaining tributaries, had improvement, with reduction in volume of about one-third and one arm returned to normal. Details of the pre- and postoperative management are included as well as a summary of the operative technique. In 3 patients in whom decompression was incomplete there was only transient improvement.

To avoid postoperative edema the authors suggest that every effort should be made to minimize infection, to secure maximum hemostasis and to provide continuous and complete evacuation of blood, serum, liquid fat and lymph from the axilla.—Martha Mottram, M.D.

RADIOISOTOPES

RHOTON, ALBERT L., JR., EICHLING, JOHN, and TER-POGOSSIAN, MICHEL M. Comparative study of mercury-197 chlormerodrin and mercury-203 chlormerodrin for brain scanning. J. Nuclear Med., Jan., 1966, 7, 50-59. (From: Division of Neurological Surgery, Beaumont-May Institute of Neurology, and the Mallinckrodt Institute of Radiology, Washington University Medical School, St. Louis, Mo.)

Hg¹⁹⁷ chlormerodrin and Hg²⁰³ chlormerodrin were compared to determine which is the best agent for brain scanning. The two agents were compared regarding: 1) tissue penetration of emitted radiation, 2) tumor to nontumor ratio of count rates, 3) whole body and renal radiation dosimetry, and 4) clinical results.

Hg²⁰³ showed a more effective tissue penetration of its photons, a better tumor to nontumor ratio of count rates achieved, and less scattered radiation than with Hg¹⁹⁷. Hg¹⁹⁷ showed a greater number of useful photons emitted, more effective detection of the photons by the scanner crystal, more scattered radiation which added to the count rate and produced some smearing of the scan images and reduced tumor to nontumor count rates, and a lower whole body and renal radiation dose than with Hg²⁰³.

The whole body radiation dose was approximately 4 times greater with Hg^{203} than with Hg^{197} . The renal radiation dose was approximately 10 times greater with Hg^{203} than with Hg^{197} .

The clinical results between Hg¹⁹⁷ and Hg²⁰³ were comparable.

The authors believe that Hg¹⁹⁷ chlormerodrin is the more favorable agent for brain scanning due to the lower renal radiation dose. Repeat or follow-up studies can be done using Hg¹⁹⁷ due to the lower renal radiation dose.

The authors are presently studying the technetium 99m pertechnetate as a scanning agent to determine whether it is as effective as the radiomercury agents in tumor localization. Technetium 99m pertechnetate offers a reduced radiation dosage and more rapid scanning than the radiomercury agents.—Charles W. Cooley, M.D.

Quinn, James L., III, and Head, Louis R. Radioisotope photoscanning in pulmonary disease. J. Nuclear Med., Jan., 1966, 7, 1–22. (From: Departments of Radiology and Surgery, Northwestern University School of Medicine, and the Nuclear Medicine Laboratory, Chicago Wesley Memorial Hospital, Chicago, Ill.)

Vascular lung scintiscanning employing aggregates of iodinated human serum albumin has been used to

study many pulmonary diseases with varying degrees of clinical results. The inhalation scanning employing radionuclides is a recent procedure that gives a gross representation of bronchial patency.

The technique for the vascular lung scintiscanning consists of injecting 120–180 μ c I¹³¹ albumin aggregates intravenously with the patient being supine. A 3-inch rectilinear scanner with a 19-hole focusing collimator and photorecorder is used. The scanning is begun immediately with the patient usually being prone; it is started at the inferior border of the rib cage to minimize the radiation from the liver and spleen. The estimated dose to the lungs from 200 μ c of I¹³¹ albumin aggregates is 1.2 rads.

The technique for the *inhalation* lung scanning consists of placing I mc of Hg^{197} chlormerodrin, $I^{181}HSA$, or Au^{198} chloride in a micronebulizer. A Bird respirator is used. A pressure of 10 cm. of H_2O and a flow rate of 7 gives particle sizes of $2-7\mu$. The particle size is reduced to 0.5 to 3μ due to evaporation when the mist enters the bronchial tree. Less than 10 per cent of the particles are deposited in the alveoli. Tc^{99m} sulfur colloid can also be used and is preferable due to the reduced dose of irradiation.

The vascular and inhalation scannings can be done at one sitting, as the gamma energy of Tc^{99m} is 140 kev. and that of I¹³¹ is 364 kev. The detector's spectrometer setting can be changed to separate the radionuclides. The approximate lung dose from 1 mc of Au¹⁹⁸ nebulized is from 0.6 to 1.8 rads. The dose could be reduced approximately by a factor of 100 using Tc^{99m}.

All of the mechanisms of radionuclide distribution and all of the disease states in which lung scans would be of value are not known due to the relative newness of the procedures. There are a number of causes of nonuniform pulmonary blood flow other than gravity.

The authors used the combined vascular and inhalation scans to study pulmonary embolus, pulmonary emphysema, asthma, congenital cystic lung, bronchiectasis, acquired cavitary disease and bronchogenic carcinoma.

The vascular scan was positive immediately after the occurrence of a pulmonary embolus. The inhalation scan showed equal filling bilaterally which would not occur in pneumonia or atelectasis. The inhalation scan demonstrated the cysts and bullae better than the vascular scan. The vascular and inhalation scans showed a decrease to absent deposition of radioactivity in bronchiectatic areas. The inhalation scan showed very little deposition in asthmatic cases during an attack. There was a marked disproportion between the vascular and the inhalation scans in asthma. There was a marked improvement following the subsidence of the attack. There was a decreased deposition of the aggregates in the areas of primary bronchogenic carcinoma.

The conclusion is reached that vascular and inhalation lung scans are of definite value in the diagnosis

of pulmonary embolus, of some value in the study of bronchiectasis and emphysema, and are of questionable value in the study of bronchogenic carcinoma.— Charles W. Cooley, M.D.

HISADA, KIN-ICHI, HIRAKI, TATSUNOSUKE, and Ohba, Satoru. Positive delineation of human tumors with ¹³¹I human serum albumin. J. Nuclear Med., Jan., 1966, 7, 41–49. (From: Department of Radiology, School of Medicine, Kanazawa, University, Kanazawa, Japan.)

Some substances have an affinity for certain types of neoplasms and can be used for localization of the neoplasms by radioisotope labeling.

The authors used I^{III}HSA in 12 cases with proven malignant neoplasms. One mc of I^{III}HSA was given intravenously to each of the 12 cancer patients, and scans were obtained at 3, 24 and 48 hours. The thyroid was blocked by the administration of 15 mg. of NaI 24 hours before and for I week after the study. The scintiscanner had a 2×2 inch sodium iodide crystal and a 37-hole lead collimator.

There was good delineation of the tumors in 4 cases: squamous cell carcinoma of the maxillary sinus, femoral metastasis from a squamous cell carcinoma of the lung, giant cell tumor of the femur, and cutaneous metastases of a lower leg from an undifferentiated cell carcinoma of the lung. There was fair tumor delineation in 2 cases: squamous cell carcinoma of the larynx and reticulum cell carcinoma of the neck. Poor delineation was shown in 3 cases: undifferentiated cell carcinoma of the lung, hepatocellular liver carcinoma, and adenocarcinoma of the kidney. There was no tumor delineation in 3 cases: metastatic cancer of the pelvis from a mixed parotid tumor, metastatic cancer of the pelvis from an adenocarcinoma of the lung, and a Virchow's node metastasis from an adenocarcinoma of the ovary.

Positive tumor delineation was best in the thin parts of the body. One mc of I^{III}HSA gives a total body radiation dose of approximately 3 rads and is considered too large to be used for a routine diagnostic procedure.

The authors are endeavoring to increase the efficiency of malignant tumor detection by improving the scintiscanner and thus lowering the radiation dose and by searching for substances with higher tumor specificity.—Charles W. Cooley, M.D.

HERMANN, GEORGE, III, and CUSTER, R. PHILIP. Splenic scintiscans with merisoprol Hg 197: a new radioactive pharmaceutical agent. J.A.M.A., March 21, 1966, 195, 1015—1019. (Address: Dr. Hermann, 51 N. 39th Street, Philadelphia, Pa. 19104.)

The ability to visualize the spleen simply, with precision, and within a relatively short time provides the

clinician with an extremely valuable diagnostic method under a wide variety of circumstances. Wagner and his group had synthesized and tested a compound labeled with Hg¹⁹⁷, now available as merisoprol Hg¹⁹⁷ (Merpane). The authors attempted 42 spleen scannings on 35 patients using Hg¹⁹⁷. Most of the subjects suffered from disorders of the blood forming organs, chiefly lukemias or lymphomas.

In lateral view the normal spleen appeared as a sharply defined area of activity averaging 75 cm.2 and was well above the left costal margin. While scanning in the anterior and posterior planes yielded complementary data regarding focal abnormalities and organ position, only the left lateral view furnished a reliable estimate of splenic size. Hepatic accumulation of the isotope was seldom a problem, in contrast to methods employing thermal damage. Liver activity averaged 25 per cent of that in the spleen and readily yielded to the "background-erase" provision of the photoscanner or to posterior scanning. Interference from renal accumulation in the anterior or posterior views was avoided by prompt initiation of scanning before renal activity was significant. The left lateral view posed no problem. These techniques provided excellent splenic visualization in 39 of 40 scans attempted among 33 patients who had not previously undergone splenectomy. The solitary nonvisualization in this group occurred in a patient with extreme thrombocythemia suspected of having sustained total splenic infarction. None of the patients experienced any immediate ill effects or sequelae incident to the agent's use, and the splenic scanning lent itself readily to out-patient use.

A detailed summary of results and 3 case reports are included.—Douglas S. Kellogg, M.D.

Weiss, Thomas E., Maxfield, William S., Murison, Paul J., and Hidalgo, John U. Scintillation scanning in rheumatoid arthritis. South. M. J., April, 1966, 59, 484–488. (From: Departments of Internal Medicine, Radiation Therapy, and Radiology, Ochsner Clinic, and the Biophysics Section of Ochsner Foundation Hospital, New Orleans, La.)

This is a report of studies of more than 100 patients with rheumatoid arthritis. The authors have found that scintillation scanning after the intravenous administration of I¹³¹HSA (25 μ c per 10 pounds body weight) or other suitable isotopes can record graphically active rheumatoid arthritis of the knees, hands, wrists, forefeet, elbows and shoulders. The scanning technique employed may show abnormal radioactivity in small joints but the resolution at present is not sufficient to pinpoint the exact area of localization of the arthritic process within these joints.

Scans of the hands and wrists and of the knees were found to be the most informative in the detec-

tion of inflammatory changes in or about the joints. In patients who had no roentgenographic evidence of inflammation, the scan aided in determining to some degree the location, extent and degree of activity of disease.

In a limited number of patients, the joint scan technique has also shown localization in gout, symptomatic osteoarthritis of the knees with synovitis, and infectious (pyogenic) arthritis.

In patients with rheumatoid arthritis, scintillation scanning furnished graphic evidence of synovitis in joints with clinically active arthritis. Positive scans were obtained in 16 per cent of patients with active rheumatoid arthritis and without roentgenographic evidence of arthritis in some joints but with positive evidence in others. Eight per cent of patients in this series had active rheumatoid arthritis, negative roentgenographic evidence of articular disease, and positive joint scans.

This method of graphically recording active rheumatoid arthritis with or without positive roent-genographic evidence of any disease may, in selected cases, be useful in evaluating the course of the disease and/or the results of therapy.—Merle K. Loken, Ph.D., M.D.

CHEMOTHERAPY

FRIEDMAN, BARRY. Chemotherapy of tuberculosis of the spine. J. Bone & Joint Surg., April, 1966, 48-A, 451-474. (Address: 2460 Fairmount Boulevard, Cleveland Heights, Ohio.)

A group of 64 patients with tuberculosis of the spine, treated without surgical fusion, by the administration of antituberculosis drugs for prolonged periods, bedrest and ambulation with braces (after serial roentgenograms demonstrated that the disease was not longer progressive), is presented.

Sixty-three patients had the usual forms of tuberculous spondylitis with involvement of the vertebral body. In the one exception the disease was localized in the posterior portion of the vertebral body and in the pedicles. Within the vertebral body itself, the disease process appeared as one of three patterns of tuberculous spondylitis. There were 57 paradiskal or metaphyseal lesions, characterized by destruction of the adjacent bone end-plates and the intervening intervertebral disk. Twenty-two anterior lesions occurred in which the anterior cortex of the body was destroyed during the active phase, but the intervertebral disk was not narrowed. Four central lesions were found wherein the vertebral body was diffusely involved during the early stages (appearing roentgenographically denser than normal) but later underwent fragmentation and collapse, the intervertebral disks not being appreciably narrowed until late.

Tuberculous abscesses were present in 48 patients in the form of paravertebral abscesses in the thoracic

spine region. Eight psoas abscesses were associated with lumbar lesions, and 4 retropharyngeal abscesses accompanied cervical spine tuberculosis. In addition, 3 patients with lesions of the thoracic spine had abscesses of the anterior chest wall, 2 with underlying rib erosion.

The number of diseased vertebrae, determined roentgenographically in each patient ranged from 1 to 6. Usually only 2 or 3 contiguous vertebrae in a spine segment contained tuberculous foci so that kyphotic deformity was rarely excessive. In several patients 2 separate areas of disease were present in the spine.

The manner in which the bone lesion underwent repair appeared to be related more to the type of tuberculous spondylitis than to the medication used. Thus the patterns of repair were identified which corresponded to each of the localizations of the disease; *i. e.* paradiskal, anterior or central.

Healing of paradiskal lesions. Serial roentgenograms and laminagrams made at intervals of approximately 3 months showed that for the first 6 months after the start of the treatment, the roentgenographic appearance was usually that of continuing bone destruction and narrowing of the intervertebral disk space. Subsequently this change was followed in some cases by a stable period of from 3 to 6 months during which there was little change in the roentgenographic appearance of the lesion. Bone repair was not evident until 6 months after the start of the treatment at the earliest; and more commonly it was seen from 9 months to I year after treatment. The roentgenographic features of repair were the appearance of fine lines of calcific density in the areas of previous bone destruction and increased bone density of the vertebral margins, particularly the anterior cortex where an osteophytic beak of new bone often appeared. At the same time the more central portions of one or both contiguous vertebral bodies occasionally appeared to be more osteoporotic than on previous roentgenograms. Over the succeeding months, however, there was evidence of a uniform increase in roentgenographic bone density, including the vertebral bodies and in most cases the intervertebral spaces as well. Finally, complete osseous interbody fusion of contiguous vertebrae occurred in 38 of the 57 paradiskal lesions. In the majority of patients, it took from 18 months to 2 years, as compared to 3-4 years using surgical fusion alone. In 14 of the paradiskal lesions, the intervertebral spaces became partially bridged with bone, the degree of bridging ranging from a narrow band to a broad zone of bone leaving only a small remnant of the intervertebral space. In 5 patients with paradiskal localization, the narrowed intervertebral space did not become bridged with bone. In each of these, the adjacent vertebral margins became distinct and in several places even sclerotic. Most of these patients were left with pockets of decreased density in one or both vertebral end-plates. These patients were followed for periods of from 4 to 8 years and since they presented no roentgenographic or clinical evidence of reactivation, it seems reasonable to assume that their disease was inactive.

Healing of anterior tuberculous spondylitis. This was the second most common form of involvement in this series. All anteriorly situated lesions healed in one of two ways—either by the formation of osteophytic bridges between adjacent vertebrae or by bone replacement of the area of destruction. Interestingly, the intervertebral disk behind the osteophytic bridge was apparently spared from infection since the space did not become narrowed on the roentgenograms.

Healing of central tuberculous spondylitis. This form occurred most frequently in childhood and only 4 cases are reported in the series. One patient failed to respond to chemotherapy and represented a single failure of treatment of a vertebral lesion in the entire series. In the other 3 patients, progression of the deformity was eventually blocked when the firm surfaces of bone beyond the area of destruction met anteriorly. In 1 patient this union was osseous while in the other 2 it appeared to be fibrous. The central localization of vertebral tuberculosis is the most destructive and therefore potentially the most deforming. If 3 or more contiguous vertebral bodies undergo the same degree of destruction, a severe kyphosis results.

Before the use of chemotherapy, when nonosseous tissue persisted between partially destroyed vertebral bodies, the arrest of disease proved to be temporary in a large number of patients. The disease often became reactivated to break down what had appeared to be a fibrous ankylosis. With the present use of chemotherapy, the response to treatment of the vertebral lesions, abscesses and sinuses is on the whole favorable. Surgical procedures for abscess evacuation and decompression laminectomy for treatment of paraplegics was carried out in some cases, but spine fusion was not performed. Isoniazid appears to be more effective than streptomycin in preventing relapses. While there are limited indications for surgical spine fusion in tuberculosis, it is not a substitute for adequate antituberculous drug therapy.—E. Nicholas Sargent, M.D.



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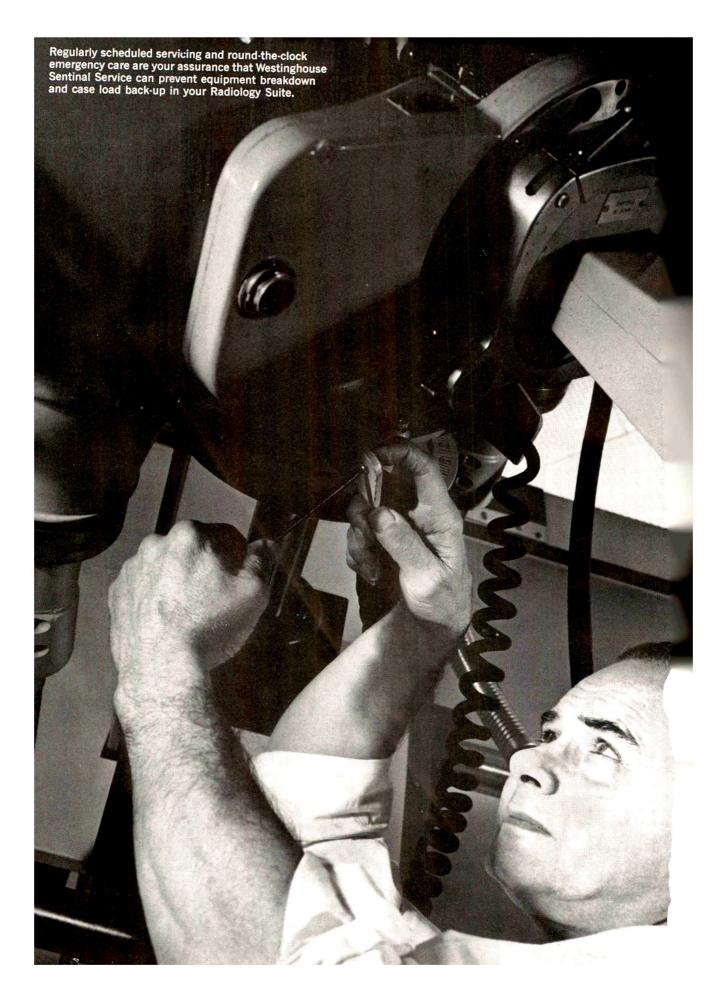
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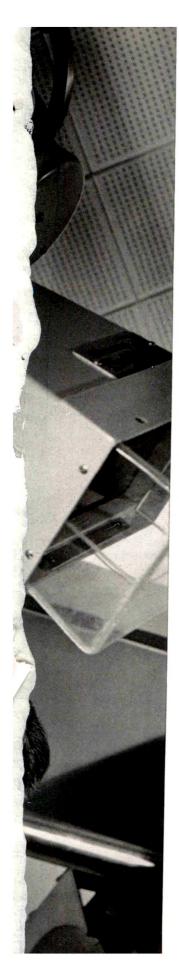
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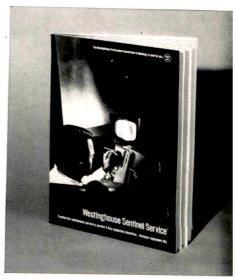
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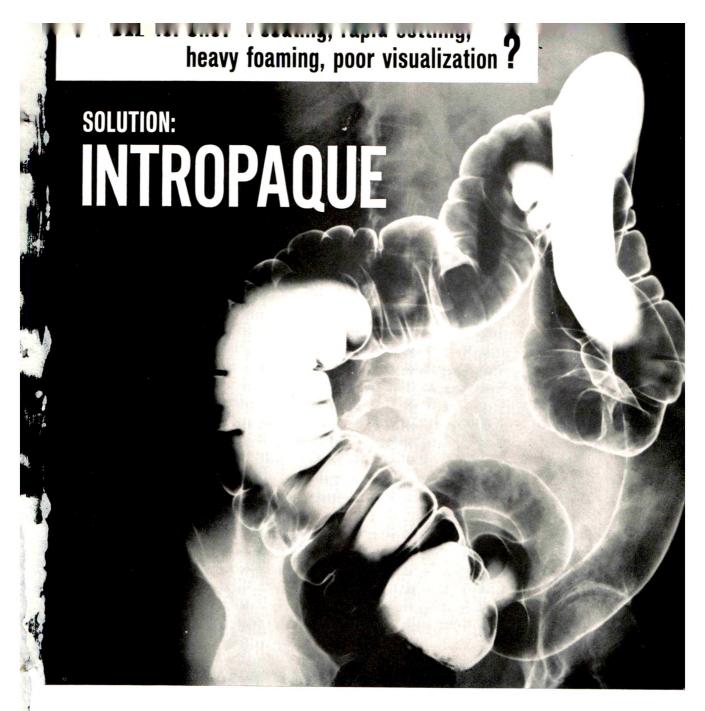
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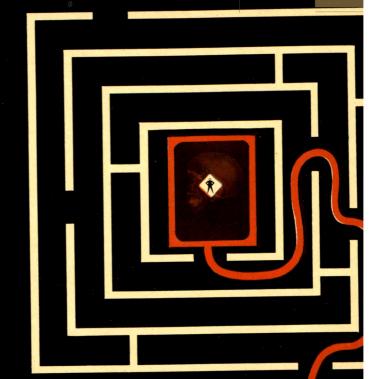
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